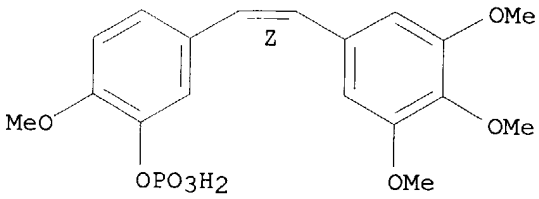
OTHER NAMES:
CN **Combretastatin A4 phosphate**
FS STEREOSEARCH
MF C18 H21 O8 P
CI COM
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, EMBASE, IMSRESEARCH, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); USES (Uses)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

40 REFERENCES IN FILE CA (1907 TO DATE)
41 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.24	13.45

FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004

FILE COVERS 1907 - 27 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 26 Sep 2004 (20040926/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> l1
L3 54 L1

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=> l2
L4            41 L2

=> l3 or l4
L5            92 L3 OR L4

=> d l5 82-92 ti

L5   ANSWER 82 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Anti-vascular approaches to solid tumor therapy: evaluation of
     combretastatin A4 phosphate

L5   ANSWER 83 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Combretastatin A-4 phosphate as a tumor vascular-targeting agent: early
     effects in tumors and normal tissues

L5   ANSWER 84 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Determination of combretastatin A-4 and its drug in plasma by
     high-performance liquid chromatography

L5   ANSWER 85 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Targeting the tumor vasculature with combretastatin A-4 disodium
     phosphate: effects on radiation therapy

L5   ANSWER 86 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   The effect of combretastatin A-4 disodium phosphate in a C3H mouse mammary
     carcinoma and a variety of murine spontaneous tumors

L5   ANSWER 87 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Effects of combretastatin on murine tumors monitored by 31P MRS, 1H MRS
     and 1H MRI

L5   ANSWER 88 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents. 389. New syntheses of the combretastatin A-4
     prodrug

L5   ANSWER 89 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate

L5   ANSWER 90 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Combretastatin A-4, an agent that displays potent and selective toxicity
     toward tumor vasculature

L5   ANSWER 91 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Combretastatin A-4 prodrug

L5   ANSWER 92 OF 92  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs


=> nucleotide
        358966 NUCLEOTIDE
        107591 NUCLEOTIDES
L6      410638 NUCLEOTIDE
                 (NUCLEOTIDE OR NUCLEOTIDES)

=> l5 and l6
L7            4 L5 AND L6

=> d l7 1-4 ti

L7   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Methods for quantifying ratio between two nucleic acids by NASBA for
```

diagnosis and treatment of HIV-1, tumor or angiogenic disorders

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods for quantifying ratio between two nucleic acids by NASBA for diagnosis and treatment of HIV-1, tumor or angiogenic disorders

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
TI Compositions and methods for treating cancer using maytansinoid CD44 antibody immunoconjugates and chemotherapeutic agents

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
TI Effects of combretastatin on murine tumors monitored by 31P MRS, 1H MRS and 1H MRI

=> d l 7 4 ti fbib abs
4 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):end

=> d l7 4 ti fbib abs

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
TI Effects of combretastatin on murine tumors monitored by 31P MRS, 1H MRS and 1H MRI
AN 1999:5891 CAPLUS
DN 130:204769
TI Effects of combretastatin on murine tumors monitored by 31P MRS, 1H MRS and 1H MRI
AU Maxwell, R. J.; Pharm, B.; Nielsen, F. U.; Breidahl, T.; Stodkilde-Jorgensen, H.; Horsman, M. R.
CS Gray Laboratory Cancer Research Trust, Northwood, HA6 2JR, UK
SO International Journal of Radiation Oncology, Biology, Physics (1998), 42(4), 891-894
CODEN: IOBPD3; ISSN: 0360-3016
PB Elsevier Science Inc.
DT Journal
LA English
AB Combretastatins have tubulin-binding activity and are being investigated for their toxicity against tumor vasculature. We report the use of 31P and 1H magnetic resonance (MR) spectroscopy and 1H MR imaging for monitoring the effects of combretastatin A-4 prodrug (100mg/kg, i.p.) on energy metabolism and necrosis, resp., in the C3H murine mammary tumor. The tumors (volume ca. 200mm3) were grown in the hind foot of mice. MR examns. were performed without anesthesia within a 7.1 T magnet. 31P MRS (TR = 6 s) was performed before treatment and at 1-, 2-, 3-, and 24-h after injection of drug or saline via an i.p. line. 1H MRS (PRESS; 24μl voxel; TR = 2 s; TE = 135 ms) and both T1-weighted (TR = 0.2 s; TE = 0.02 s) and T2-weighted (TR = 2 s; TE = 0.20 s) 1H MRI were performed before treatment and 2.5 and 24 h afterwards. The ratio β-**nucleotide** triphosphate/inorg. phosphate fell by 33% within 1 h of treatment and remained constant for a further 2 h. A small but significant fall in pH (by 0.11 units) was observed at 1 h. Although an increase in the 1H MR spectroscopy signal at about 1.32 ppm (predominantly from lactate) was observed in some tumors following combretastatin treatment, this effect was not seen consistently. No changes in the intensity of T2-weighted 1H MR images or in tumor necrosis (measured histol.) were detected within 3 h of treatment. The reduction in tumor energetics and pH was consistent with a reduction in tumor blood flow but this occurred before any significant incidence of haemorrhagic necrosis was detected. The combretastatin dose used to achieve these effects was less than one tenth of the maximum tolerated dose in mice.
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> lithium
        280916 LITHIUM
           352 LITHIUMS
L8      281040 LITHIUM
                 (LITHIUM OR LITHIUMS)

=> d his

     (FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 07:15:56 ON 27 SEP 2004
               E COMBRETASTATIN A-4/CN
L1             1 E9
L2             1 E10

     FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3            54 L1
L4            41 L2
L5            92 L3 OR L4
L6        410638 NUCLEOTIDE
L7             4 L5 AND L6
L8        281040 LITHIUM

=> l5 and l8
L9             3 L5 AND L8

=> d l19 1-3 ti
L19 NOT FOUND
The L-number entered has not been defined in this session, or it
has been deleted.  To see the L-numbers currently defined in this
session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d l9 1-3 ti

L9   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Methods of synthesizing prodrugs of combretastatin A-4

L9   ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Synthesis of hydroxyphenstatin and the prodrugs thereof as anticancer and
     antimicrobial agents

L9   ANSWER 3 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents 429. Syntheses of the combretastatin A-1 and
     combretastatin B-1 prodrugs


=> d l9  3 ti fbib abs

L9   ANSWER 3 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents 429. Syntheses of the combretastatin A-1 and
     combretastatin B-1 prodrugs
AN   2000:757705  CAPLUS
DN   134:51116
TI   Antineoplastic agents 429. Syntheses of the combretastatin A-1 and
     combretastatin B-1 prodrugs
AU   Pettit, George R.; Lippert, John W., III
CS   Cancer Research Institute and Department of Chemistry and Biochemistry,
     Arizona State University, Tempe, AZ, 85287-2404, USA
SO   Anti-Cancer Drug Design (2000), 15(3), 203-216
     CODEN: ACDDEA; ISSN: 0266-9536
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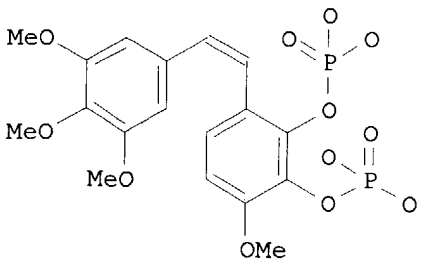
PB Oxford University Press
DT Journal
LA English
GI



I

AB The original synthesis of combretastatin A-1 was modified to allow an efficient scale-up procedure for obtaining this antineoplastic stilbene. Subsequent conversion to a useful prodrug was accomplished by diphosphorylation, with in situ formation of dibenzylchlorophosphite, followed by cleavage of the benzyl ester protecting groups with trimethyliodosilane. The phosphoric acid intermediate was treated with sodium methoxide to complete a practical route to the sodium phosphate prodrug (I). Selective hydrogenation of phosphate derivative and treatment of the product with sodium methoxide led to combretastatin B-1 prodrug. The phosphoric acid precursor of prodrug I was employed in a parallel series of reactions to produce a selection of metal and ammonium cation prodrug candidates. Each of the phosphate salts was evaluated from the perspective of relative solubility behavior and cancer cell growth inhibition. The sodium phosphate prodrug I was selected for detailed antineoplastic studies.

RE.CNT 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

FILE 'REGISTRY' ENTERED AT 07:15:56 ON 27 SEP 2004
E COMBRETASTATIN A-4/CN
L1 1 E9
L2 1 E10

FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3 54 L1
L4 41 L2
L5 92 L3 OR L4
L6 410638 NUCLEOTIDE
L7 4 L5 AND L6
L8 281040 LITHIUM
L9 3 L5 AND L8

=> 15/prep
FIELD CODES CANNOT BE CHANGED HERE
You may have tried to apply a field code to a term that already has a field code. You can only add a field code to a term that has no field code appended to it.

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=> l1/prep
            54 L1
       3201185 PREP/RL
L10           8 L1/PREP
                  (L1 (L) PREP/RL)

=> d l10 1-8 ti

L10  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of resveratrol and sodium resverastatin phosphate derivatives
     for use in pharmaceutical compositions as antineoplastic and antimicrobial
     agents

L10  ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Synthesis of disodium combretastatin A-4 3'-O-phosphate

L10  ANSWER 3 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Methods of synthesizing prodrugs of combretastatin A-4

L10  ANSWER 4 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation and formulation of combretastatin A4 prodrugs and their
     trans-isomers for use as antitumor agents

L10  ANSWER 5 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents. 389. New syntheses of the combretastatin A-4
     prodrug

L10  ANSWER 6 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate

L10  ANSWER 7 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Combretastatin A-4 prodrug

L10  ANSWER 8 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs


=> d l10 8 ti fbib abs

L10  ANSWER 8 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs
AN   1995:661775  CAPLUS
DN   123:227731
TI   Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs
AU   Pettit, George R.; Temple, Carroll, Jr.; Narayanan, Ven L.; Varma, Ravi;
     Simpson, Michael J.; Boyd, Michael R.; Rener, Gregory A.; Bansal, Namita
CS   Cancer Research Institute and Department of Chemistry, Arizona State
     University, Temple, AZ, 85287-1604, USA
SO   Anti-Cancer Drug Design (1995), 10(4), 299-309
     CODEN: ACDDEA; ISSN: 0266-9536
PB   Oxford University Press
DT   Journal
LA   English
GI
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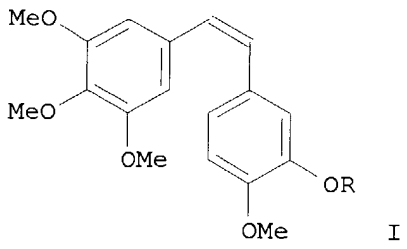

I

AB Combretastatin A-4 (I, R = H), the principal cancer cell growth-inhibitory constituent of the Zulu medicinal plant (Combretum caffrum, has been undergoing preclin. development. However, the very limited water solubility of this phenol has complicated drug formation. Hence, derivs. of the combretastatin A-4 3'-phenol group were prepared for evaluation as possible water-soluble prodrugs. As observed for combretastatin A-4, the sodium salt (I,
R = Na), potassium salt (I, R = K), and hemisuccinic acid ester (I, R = COCH2CH2CO2H) derivs. were essentially insol. in water. Indeed, these substances regenerated combretastatin A-4 upon reaction with water. A series of other simple derivs., e.g. I [R = COCH(NH2)CH2CH2CO2H], proved unsatisfactory in terms of water solubility or stability, or both. The most soluble derivs. evaluated included the ammonium [I, R = P(O)(OH)ONH4], and potassium [I, R = P(O)(OK)2] and sodium [I, R = P(O)(ONa)2] phosphate salts, where the latter two proved most stable and suitable. Both the potassium and sodium phosphate derivs. of combretastatin A-4 were also found to exhibit the requisite biol. properties necessary for a useful prodrug. The sodium phosphate salt was selected for drug formulation and further pre-clin. development.

=> d l10 7 ti fbib abs

L10 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
TI Combretastatin A-4 prodrug
AN 1996:616598 CAPLUS
DN 125:309027
TI Combretastatin A-4 prodrug
IN Pettit, George R.
PA Arizona State University, USA
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5561122	A	19961001	US 1994-363406	19941222
				US 1994-363406	19941222

AB Disclosed herein are combretastatin A4 prodrugs with improved water solubility and stability, for the treatment of one or more neoplastic diseases by means of chemotherapy. Disodium combretastatin A4 3-O-phosphate (I) was prepared and combretastatin A4 and I demonstrated similar in vitro activity levels in the NCI 60 cell line panel. Formulations containing the prodrugs are provided.

=> logoff hold
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	37.80	51.25

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -2.80      -2.80

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 07:36:27 ON 27 SEP 2004

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 07:43:42 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 07:43:42 ON 27 SEP 2004
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COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  37.80      51.25

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -2.80      -2.80

=> FIL STNGUIDE
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  38.24      51.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -2.80      -2.80

FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 24, 2004 (20040924/UP).

=> DIS SAVED
NAME             CREATED      NOTES/TITLE
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ALKYLATIN/L      13 DEC 2001  9 L-NUMBERS
ESTERODOR/L      05 SEP 2002  42 L-NUMBERS
GABACOMPDS/A     TEMP         45 ANSWERS IN FILE CAPLUS
GORDSRCH/L       TEMP         30 L-NUMBERS
INDIUMCL3/A      30 MAY 2001  1 ANSWER IN FILE REGISTRY
LTWENTAUGFOR/A   04 AUG 2001  72 ANSWERS IN FILE CAPLUS
NEOTAMECRYST/A   24 APR 2001  59 ANSWERS IN FILE CAPLUS
NVLARMFULGEN/A   19 APR 2001  196 ANSWERS IN FILE REGISTRY
POHBENZALDEH/A   10 JUL 2001  5519 ANSWERS IN FILE CAPLUS
PROSTACMPD15/A   01 AUG 2001  34 ANSWERS IN FILE CAPLUS
STILLEAPP/L      07 JAN 2002  17 L-NUMBERS
TWOAMINOPOLY/Q   16 APR 2001  UPLOADED STRUCTURE
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=> DIS SAVED/S
NO SAVED SDI REQUESTS


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NAME             CREATED      NOTES/TITLE
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ALKYLATIN/L      13 DEC 2001  9 L-NUMBERS
ESTERODOR/L      05 SEP 2002  42 L-NUMBERS
GABACOMPDS/A     TEMP         45 ANSWERS IN FILE CAPLUS
GORDSRCH/L       TEMP         30 L-NUMBERS
INDIUMCL3/A      30 MAY 2001  1 ANSWER IN FILE REGISTRY
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NVLARMFULGEN/A   19 APR 2001  196 ANSWERS IN FILE REGISTRY
POHBENZALDEH/A   10 JUL 2001  5519 ANSWERS IN FILE CAPLUS
PROSTACMPD15/A   01 AUG 2001  34 ANSWERS IN FILE CAPLUS
STILLEAPP/L      07 JAN 2002  17 L-NUMBERS
TWOAMINOPOLY/Q   16 APR 2001  UPLOADED STRUCTURE


=> DIS SAVED/S
NO SAVED SDI REQUESTS


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=> DEL ESTERODOR/L
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=> DEL GORDSRCH/L
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=> DEL INDIUMCL3/A
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=> DEL LTWENTAUGFOR/A
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=> DEL PROSTACMPD15/A
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=> DEL STILLEAPP/L
DELETE STILLEAPP/L? (Y)/N:Y

=> d his

     (FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)
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     FILE 'REGISTRY' ENTERED AT 07:15:56 ON 27 SEP 2004
                E COMBRETASTATIN A-4/CN
L1             1 E9
L2             1 E10

     FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3            54 L1
L4            41 L2
L5            92 L3 OR L4
L6        410638 NUCLEOTIDE
L7             4 L5 AND L6
L8        281040 LITHIUM
L9             3 L5 AND L8
L10            8 L1/PREP

     FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
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                DEL ESTERODOR/L
                DEL GABACOMPDS/A
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                DEL LTWENTAUGFOR/A
                DEL NEOTAMECRYST/A
                DEL NVLARMFULGEN/A
                DEL POHBENZALDEH/A
                DEL PROSTACMPD15/A
                DEL STILLEAPP/L

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.24      51.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -2.80

FILE 'REGISTRY' ENTERED AT 07:46:20 ON 27 SEP 2004
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STRUCTURE FILE UPDATES:   24 SEP 2004  HIGHEST RN 751457-34-8
DICTIONARY FILE UPDATES:  24 SEP 2004  HIGHEST RN 751457-34-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e tetrabromomethane/cn
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E4              1      TETRABROMOMETHANE COMPD. WITH N,N,N',N'-TETRABENZYL-4,4'-DIA
                       MINODIPHENYLMETHANE/CN
E5              1      TETRABROMOMETHANE COMPD. WITH N,N,N',N'-TETRAMETHYL-4,4'-DIA
                       MINODIPHENYLMETHANE/CN
E6              1      TETRABROMOMETHANE RADICAL CATION/CN
E7              1      TETRABROMOMETHANE RADICAL ION(1-)/CN
E8              1      TETRABROMOMETHANE-13C/CN
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E10             1      TETRABROMONAPHTHALENE-2,3-DICARBOXYLIC ANHYDRIDE/CN
E11             1      TETRABROMONEOPENTANE/CN
E12             1      TETRABROMONICKELATE(2-)/CN

=> e3
L11             1 TETRABROMOMETHANE/CN

=> e tetrachloromomethane/cn
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E2              1      TETRACHLOROMETHYLTANTALUM/CN
E3              0 --> TETRACHLOROMOMETHANE/CN
E4              1      TETRACHLORONAPHTHALENE/CN
E5              1      TETRACHLORONAPHTHALENE-2,3-DICARBOXIMIDE/CN
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E7              1      TETRACHLORONAPHTHAZARIN/CN
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E12             1      TETRACHLORONICOTINOYL CHLORIDE/CN

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E8              1      TETRACHLOROMETHANE RADICAL ION(1-)/CN
E9              1      TETRACHLOROMETHANE(1+)/CN
E10             1      TETRACHLOROMETHANE-13C/CN
E11             1      TETRACHLOROMETHANE-VINYL ACETATE TELOMER/CN
E12             1      TETRACHLOROMETHANE-VINYL CHLORIDE TELOMER/CN

=> e3
L12             1 TETRACHLOROMETHANE/CN

=> e tetraiodomethane/cn
E1              1      TETRAIODOMAGNESATE(2-)/CN
E2              1      TETRAIODOMERCURATE(2-)/CN
E3              1 --> TETRAIODOMETHANE/CN
E4              1      TETRAIODOMETHANE DICATION/CN
E5              1      TETRAIODOMETHYLENE BLUE IODATE/CN
E6              1      TETRAIODONEOPENTANE/CN
E7              1      TETRAIODONICKELATE(2-)/CN
E8              1      TETRAIODOOXALATOOSMATE(2-)/CN
E9              1      TETRAIODOPALLADATE(2-)/CN
E10             1      TETRAIODOPHENOL BLUE/CN
E11             1      TETRAIODOPHENOLPHTHALEIN DISODIUM SALT/CN
E12             1      TETRAIODOPHENOLPHTHALEIN DISODIUM SALT TRIHYDRATE/CN

=> e3
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L13 1 TETRAIODOMETHANE/CN

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	14.97	66.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-2.80

FILE 'CAPLUS' ENTERED AT 07:48:31 ON 27 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 26 Sep 2004 (20040926/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> l11
L14 2953 L11

=> l12
L15 40657 L12

=> l13
L16 325 L13

=> l14 or l15 or l16
L17 42754 L14 OR L15 OR L16

=> ?phosphite
L18 39583 ?PHOSPHITE

=> l17 and l18
L19 207 L17 AND L18

=> l17 and l18
L20 207 L17 AND L18

=>

=>

=>

=> l17(l)l18
L21 52 L17(L)L18

```
=> combrestatin
             4 COMBRESTATIN
             2 COMBRESTATINS
L22          4 COMBRESTATIN
                 (COMBRESTATIN OR COMBRESTATINS)

=> combretastatin
           430 COMBRETASTATIN
            62 COMBRETASTATINS
L23        437 COMBRETASTATIN
                 (COMBRETASTATIN OR COMBRETASTATINS)

=> l21 and l23
L24          0 L21 AND L23

=> d his

     (FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 07:15:56 ON 27 SEP 2004
                 E COMBRETASTATIN A-4/CN
L1             1 E9
L2             1 E10

     FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3            54 L1
L4            41 L2
L5            92 L3 OR L4
L6        410638 NUCLEOTIDE
L7             4 L5 AND L6
L8        281040 LITHIUM
L9             3 L5 AND L8
L10            8 L1/PREP

     FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
                 DEL ALKYLATIN/L
                 DEL ESTERODOR/L
                 DEL GABACOMPDS/A
                 DEL GORDSRCH/L
                 DEL INDIUMCL3/A
                 DEL LTWENTAUGFOR/A
                 DEL NEOTAMECRYST/A
                 DEL NVLARMFULGEN/A
                 DEL POHBENZALDEH/A
                 DEL PROSTACMPD15/A
                 DEL STILLEAPP/L

     FILE 'REGISTRY' ENTERED AT 07:46:20 ON 27 SEP 2004
                 E TETRABROMOMETHANE/CN
L11            1 E3
                 E TETRACHLOROMOMETHANE/CN
                 E TETRACHLOROMETHANE/CN
L12            1 E3
                 E TETRAIODOMETHANE/CN
L13            1 E3

     FILE 'CAPLUS' ENTERED AT 07:48:31 ON 27 SEP 2004
L14         2953 L11
L15        40657 L12
L16          325 L13
L17        42754 L14 OR L15 OR L16
L18        39583 ?PHOSPHITE
```

```
L19          207 L17 AND L18
L20          207 L17 AND L18
L21           52 L17(L)L18
L22            4 COMBRESTATIN
L23          437 COMBRETASTATIN
L24            0 L21 AND L23

=> l23 and l18
L25          19 L23 AND L18

=> d l25 10-19 ti

L25  ANSWER 10 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of trimethoxyphenyl-containing tubulin binding ligands and
     corresponding prodrug constructs as inhibitors of tubulin polymerization
     and antimitotic agents

L25  ANSWER 11 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of indole-containing and combretastatin-related
     anti-mitotic and anti-tubulin polymerization agents

L25  ANSWER 12 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents 429. Syntheses of the combretastatin A-1
     and combretastatin B-1 prodrugs

L25  ANSWER 13 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic Agents. 443. Synthesis of the Cancer Cell Growth Inhibitor
     Hydroxyphenstatin and Its Sodium Diphosphate Prodrug

L25  ANSWER 14 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation and formulation of combretastatin A4 prodrugs and
     their trans-isomers for use as antitumor agents

L25  ANSWER 15 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Synthesis and formulation of phenstatin and related prodrugs for use as
     antitumor agents

L25  ANSWER 16 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents 393. Synthesis of the trans-isomer of
     combretastatin A-4 prodrug

L25  ANSWER 17 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents. 389. New syntheses of the combretastatin
     A-4 prodrug

L25  ANSWER 18 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate

L25  ANSWER 19 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   α-Aryl-α-(2-tetrahydropyranyloxy)methanephosphonates as
     reagents in the Horner reaction.  A simple novel synthesis of (±)-
     combretastatin


=> l17 and l19
L26         207 L17 AND L19

=> l18 and l23
L27          19 L18 AND L23

=> d l2514-19 ti fbib abs
'L2514-19' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'
```

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,
e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> d 127 14-19 ti fbib abs

L27 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of **combretastatin** A4 prodrugs and their trans-isomers for use as antitumor agents
AN 1999:451301 CAPLUS
DN 131:73507
TI Preparation and formulation of **combretastatin** A4 prodrugs and their trans-isomers for use as antitumor agents
IN Pettit, George R.; Rhodes, Monte R.
PA Arizona State University, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI WO 9935150	A1	19990715	WO 1999-US419		19990108
W: CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
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			US 1998-111531P	P	19981209
CA 2314238	AA	19990715	CA 1999-2314238		19990108
			US 1998-71070P	P	19980109
			US 1998-111531P	P	19981209
			WO 1999-US419	W	19990108
EP 1045853	A1	20001025	EP 1999-902121		19990108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
			US 1998-71070P	P	19980109
			US 1998-111531P	P	19981209
			WO 1999-US419	W	19990108
JP 2002500227	T2	20020108	JP 2000-527548		19990108
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			US 1998-111531P	P	19981209
			WO 1999-US419	W	19990108

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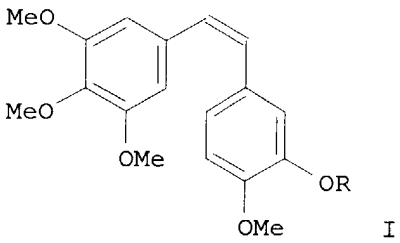

I

AB **Combretastatin** A4 I (R = H) and analogous phosphate prodrugs I [R = PO(OR1)OR2; R1, R2 = H, Na, Ca, Cs, Li, Mg, Mn, Zn, imidazole, morpholine, piperazine piperidine, pyrazole, pyridine, adenosine, cinchonine, glucosamine quinine, quinidine, tetracycline, verapamil; R1 = R2 = H, benzyl] and (E)-**Combretastatin** A4 phosphate analogs were prepared and formulated for use as water soluble antineoplastic agents. Thus, **combretastatin** A4 was reacted with dibenzyl **phosphite** to give dibenzyl ester I [R = P(O)(OCH2Ph)2] in 98% yield. Also, **combretastatin** A4 was converted to the sodium phosphate salt I [R = PO3HNa] via the formation of the silylethyl ester I [R = P(O)(OCH2CH2SiMe3)2]. The **combretastatin** A4 phosphate esters were tested for antitumor activity against a variety of cancer cell lines and were also tested for antimicrobial activity against bacterial and fungal strains.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis and formulation of phenstatin and related prodrugs for use as antitumor agents
AN 1999:451177 CAPLUS
DN 131:73506
TI Synthesis and formulation of phenstatin and related prodrugs for use as antitumor agents
IN Pettit, George R.; Toki, Brian
PA Arizona State University, USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI	WO 9934788	A1	19990715	WO 1999-US475		19990109
	W: CA, JP, US					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
				US 1998-70878P	P	19980109
	CA 2314510	AA	19990715	CA 1999-2314510		19990109
				US 1998-70878P	P	19980109
				WO 1999-US475	W	19990109
	EP 1045689	A1	20001025	EP 1999-902133		19990109
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
				US 1998-70878P	P	19980109
				WO 1999-US475	W	19990109
	JP 2002500184	T2	20020108	JP 2000-527239		19990109
				US 1998-70878P	P	19980109
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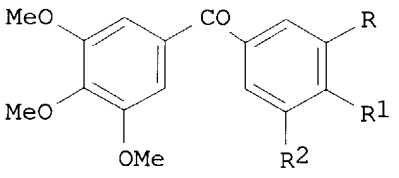
OS MARPAT 131:73506
GI



I

AB Phenstatin I (R = H, R1 = OMe, R2 = OH) and related prodrugs I [R = H, OMe, Me, Cl, F; R1 = H, OMe; R2 = OPO3Na2, OPO3H2, OAc, OMe, Me, Cl, F; R1R2 = OCH2O] were prepared and formulated for use as antineoplastic agents. Thus, phenstatin was converted to the sodium phosphate prodrug I (R = H, R1 = OMe, R2 = OPO3Na2) by a **dibenzylphosphite** phosphorylation and subsequent hydrogenolysis sequence. Phenstatin was found to be a potent inhibitor of tubulin polymerization and the binding of colchicine to tubulin comparable to **combretastatin** A-4.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 393. Synthesis of the trans-isomer of **combretastatin** A-4 prodrug
AN 1999:284035 CAPLUS
DN 131:82669

TI Antineoplastic agents 393. Synthesis of the trans-isomer of **combretastatin** A-4 prodrug

AU Pettit, George R.; Rhodes, Monte R.; Herald, Delbert L.; Chaplin, Dai J.; Stratford, Michael R. L.; Hamel, Ernest; Pettit, Robin K.; Chapuis, Jean-Charles; Oliva, Deanna

CS Cancer Research Institute and Department of Chemistry, Arizona State University, Tempe, AZ, 85287-2494, USA

SO Anti-Cancer Drug Design (1998), 13(8), 981-993
CODEN: ACDDEA; ISSN: 0266-9536

PB Oxford University Press

DT Journal

LA English

AB The (E)-stilbene isomer (2a) of the (Z)-**combretastatin** A-4 prodrug (1b) was efficiently prepared from (E)-**combretastatin** A-4 by a reaction sequence employing phosphorylation (dibenzyl **chlorophosphite**), cleavage (trimethyliodosilane) of the benzyl ester and reaction of the resulting phosphoric acid with sodium methoxide. The sodium phosphate product (2c) was also found to be an important side-product, presumably from iodine-catalyzed isomerization, when the analogous synthetic route was used to obtain the **combretastatin** A-4 prodrug (1b). The phosphoric acid precursor of prodrug 1b derived from (Z)-**combretastatin** A-4 (1a) was converted into a series of metal cation and ammonium cation salts to evaluate effects on human cancer cell growth, antimicrobial activities and solubility behavior.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

TI Antineoplastic agents. 389. New syntheses of the **combretastatin** A-4 prodrug

AN 1998:301433 CAPLUS

DN 129:36213

TI Antineoplastic agents. 389. New syntheses of the **combretastatin** A-4 prodrug

AU Pettit, George R.; Rhodes, Monte R.

CS Cancer Research Institute and Department of Chemistry, Arizona State University, Tempe, AZ, 85287-2404, USA

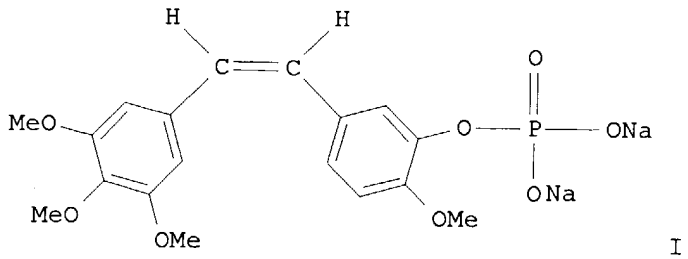
SO Anti-Cancer Drug Design (1998), 13(3), 183-191
CODEN: ACDDEA; ISSN: 0266-9536

PB Oxford University Press

DT Journal

LA English

GI

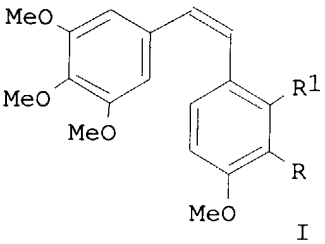


I

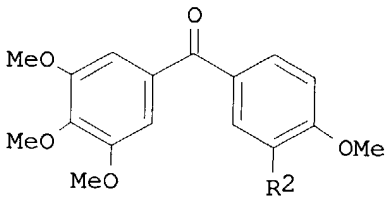
AB **Combretastatin** A-4 as the phosphate ester prodrug I is a potent antineoplastic and antiangiogenesis substance and is in advanced preclin. development. For the purpose of improving the phosphorylation synthetic sequence from **combretastatin** A-4, new routes were studied. The phosphorylation step is considerably improved using in situ-generated dibenzyl **chlorophosphite**. Cleavage of the benzyl esters

employing a trimethylchlorosilane/NaI procedure, followed by treatment with Na methoxide, led to the water-soluble prodrug I in high yield.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate
AN 1998:253141 CAPLUS
DN 128:230173
TI Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate
AU Pettit, George R.; Toki, Brian; Herald, Delbert L.; Verdier-Pinard, Pascal; Boyd, Michael R.; Hamel, Ernest; Pettit, Robin K.
CS Cancer Research Institute and Department of Chemistry, Arizona State University, Tempe, AZ, 85287-1604, USA
SO Journal of Medicinal Chemistry (1998), 41(10), 1688-1695
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I



II

AB A structure-activity relationship (SAR) study of the South African willow tree (Combretum caffrum) antineoplastic constituent **combretastatin** A-4 (I; R = OH, R1 = H) directed at maintaining the (Z)-stilbene relationship of the olefin di-Ph substituents led to synthesis of a potent cancer cell growth inhibitor designated phenstatin (II; R2 = OH). Initially phenstatin silyl ether (II; R2 = OSiMe2CMe3) was unexpectedly obtained by Jacobsen oxidation of **combretastatin** A-4 silyl ether (I; R = OSiMe2CMe2, R1 = H), and the parent phenstatin (II; R2 = OH) was later synthesized in quantity. Phenstatin was converted to the sodium phosphate prodrug [II; R2 = OP(O)(ONa)2] by a dibenzyl **phosphite** phosphorylation and subsequent hydrogenolysis sequence. Phenstatin (II; R2 = OH) inhibited growth of the pathogenic bacterium Neisseria gonorrhoeae and was a potent inhibitor of tubulin polymerization and the binding of colchicine to tubulin comparable to **combretastatin** A-4 (I; R = OH, R1 = H). Interestingly, the prodrugs were found to have reduced activity in these biochem. assays. While no significant tubulin activity was observed with the phosphorylated derivative of **combretastatin** A-4 (I; R = OH, R1 = H), phosphate II [R2 = OP(O)(ONa)2] retained detectable inhibitory effects in both assays.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

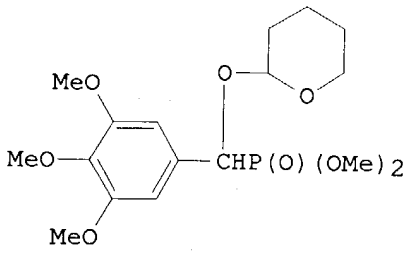
L27 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI α-Aryl-α-(2-tetrahydropyranyloxy)methanephosphonates as reagents in the Horner reaction. A simple novel synthesis of (±)-**combretastatin**
AN 1989:94838 CAPLUS
DN 110:94838

TI α-Aryl-α-(2-tetrahydropyranyloxy)methanephosphonates as reagents in the Horner reaction. A simple novel synthesis of (±)-**combretastatin**

AU Napolitano, Elio; Fiaschi, Rita; Marsili, Antonio
CS Ist. Chim. Org., Fac. Farm., Pisa, I-56100, Italy

SO Gazzetta Chimica Italiana (1988), 118(5), 415-16
CODEN: GCITA9; ISSN: 0016-5603
DT Journal
LA English
OS CASREACT 110:94838

GI



I

AB (±)-**Combretastatin** has been synthesized on 34% yield from 3,4,5-(MeO)3C6H2CHO. The key step involves Horner condensation of 4,3-MeO(MeOCH2O)C6H3CHO with methanephosphate I followed by acid hydrolysis to give 3,4,5-(MeO)3C6H2COCH2C6H3(OH)OMe-3,4.

=>
=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	40.14	107.04
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.20	-7.00

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:10:32 ON 27 SEP 2004

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 08:12:18 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 08:12:18 ON 27 SEP 2004

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	40.14	107.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.20	-7.00

=> help dt
HELP FOR 'DT' IS NOT AVAILABLE
For information about help messages available in all files, enter "HELP MESSAGES". For information about help messages available for the current file, enter "HELP DIRECTORY". For a list of commands, enter "HELP COMMANDS".

=> help document type
HELP FOR 'DOCUMENT TYPE' IS NOT AVAILABLE
For information about help messages available in all files, enter "HELP MESSAGES". For information about help messages available for the current file, enter "HELP DIRECTORY". For a list of commands, enter "HELP COMMANDS".

=> help help
The HELP command is used to view explanations of commands, formats, etc., at your terminal. To use this command, enter "HELP" and the name of the item you want explained. The system will display an explanation of how to use the item.

Example:
   => HELP DISPLAY (For help with the DISPLAY command).

For a list of commands, enter "HELP COMMANDS". For a list of online explanations, enter "HELP MESSAGES".

Help is also available at any prompt, and after any error message. Enter "HELP" or "?" at a prompt to see an explanation of the options. After an error message, enter "HELP" or "?" at the next prompt and you will receive a more detailed explanation of the error and how to correct it.

Automatic help is also available. When the SET parameter AUHELP is 'ON', you will automatically receive help following an error message. For more information on the SET parameter AUHELP, enter "HELP SET AUHELP" at an arrow prompt (=>).

=> help commands
Enter one of these commands at the arrow prompt (=>).

ACTIVATE ----- Assign L#s to saved query or answer set.
ANALYZE ------ Build expand terms from answer fields.
ARCHIVE ------ Purchase rights for archiving.
DELETE ------- Delete saved or current session items.
DISPLAY ------ Display saved or current session items.
DUPLICATE ---- Determine duplicate answers
EDIT --------- Modify the text of an E-number entry.
EXPAND ------- Look at the index around a term.
FILE --------- Specify the search and display file.
FOCUS -------- Rank answers in order of relevancy.
FSEARCH ------ Find records from given patent family(s)
FSORT -------- Sort patent records by patent family
HELP --------- For help on how to use the system.
INDEX -------- Specify the Index environment.
LOGOFF ------- End the online session.
NEWS --------- Display current news about the system.
ORDER -------- Order an original document or copy.
PRINT -------- Print answers offline.
QUERY -------- Define a search question (query).

```
REDISTRIBUTE - Purchase rights for redistribution.
SAVE --------- Save an L-numbered query or answer set.
SDI ---------- Request searches be run on file updates.
SEARCH ------- Perform a search.
SELECT ------- Build expand terms from answer fields.
SET ---------- Set terminal and interaction options.
SORT --------- Sort Answers of an L-number list
TABULATE ----- Analyze SmartSELECT L-number data.
TRANSFER ----- Extract terms from answers and search.
? ------------ The same as HELP.
Enter one of these commands at the arrow prompt (=>).


For more detailed information about a command, enter HELP followed by
the command name at an arrow prompt.

Example: => HELP SEARCH

For information on entering multiple commands at a single arrow
prompt, enter HELP COMMAND STACKING.

=> help select

 The SELECT command is used to extract terms for an L-number answer
 set or a SET AUDIT L-number (an L-number created by a SEARCH of an
 L-number with SET AUDIT set to ON).  The resulting E-numbers
 may then be used for further searching.

 Enter SELECT, the L-number answer set, the display field code or
 codes, and the answer numbers.  You must be in the file where the
 answer set was created.  The valid display fields from which terms
 can be extracted and the default field are file-specific.  Enter HELP
 EFIELDS at an arrow prompt (=>) in the file for a list of valid
 fields.  You may specify a single answer, multiple answers, or a
 range of answers.  The default is answer 1-, i.e., all the answers.
 An E-number list is created with each term having the selected field
 code appended.  The list includes the number of times the extracted
 term occurred in the answer set.

 To display an E-number list, enter DISPLAY SELECT.  Enter HELP
 DISPLAY SELECT at an arrow prompt for more information.

 To use the extracted terms in a SEARCH, search the E-number of the
 relevant term or terms.

 If you wish to change the field code, use the EDIT command.  Enter
 HELP EDIT at an arrow prompt for more information.

     Example:

          => S SKYLAB AND GRATING
          L1          15 SKYLAB AND GRATING

          => SELECT L1
          ENTER ANSWER NUMBER OR RANGE (1-):.
          ENTER DISPLAY CODE (TI) OR ?:.
          E1 THROUGH E91 ASSIGNED

          => D SELECT E1-10

          E1            5     A/TI
          E2            5     SKYLAB/TI
          E3            4     EXTREME/TI
```

```
E4            4     FLARE/TI
E5            4     INCIDENCE/TI
E6            4     ULTRAVIOLET/TI
E7            3     EXPERIMENT/TI
E8            3     GRATING/TI
E9            3     MM/TI
E10           3     MULTILAYER/TI

=> S L1 AND E4
L2            4 L1 AND FLARE/TI

=> D KWIC
L2   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
TI   A two-temperature model for the flare of 5
     September, 1973
AB   . . . transfer during the x-ray flare of 18:31 GMT
     on 5 Sept., 1973 were studied using the observations
     in the objective grating mode of the AS & E
     X-ray spectrog. telescope on Skylab. The
     flare was a moderately energetic one, Class M1
     according to M1 according to Solrad. In Hα,
     however, it was. . .
```

To SELECT only hit terms from the specified answers and fields, add HIT to the SELECT command.

Example:

```
=> S SKYLAB AND GRATING
L1           15 SKYLAB AND GRATING

=> SEL HIT TI
E1 THROUGH E2 ASSIGNED

=> D SEL

E1            5     SKYLAB/TI
E2            3     GRATING/TI
```

You may use SELECT to extract terms only if they meet certain criteria. To extract terms that contain a 1-20 character string, add WITH followed by the character string in quotes to SELECT. To extract all terms that do not contain a 1-20 character string, add NOT followed by the character string in quotes to SELECT. When selecting from a SmartSELECT L-number, WITH and NOT apply to both the term and the appended field code. To extract only the first n characters of each term, add LEN n to SELECT. LEN may be used with WITH or with NOT in one SELECT command. WITH and NOT may not be used in the same SELECT command.

Examples:

```
=> SEL L5 AU 1-10 WITH "BROWN"
=> SEL L8 1- WITH "BROWN"
=> SEL L9 1- NOT "METHANE"
=> SEL L10 1- LEN 15
=> SEL L11 TOP 20 WITH "BROWN" LEN 10
```

Successive SELECT commands add to the end of previous E-number lists. If you exceed the maximum E-number, E999, you will receive a message. The message will give the number of the answer that was being processed. You can search the terms you want, delete the list using DELETE SELECT, and then use SELECT again, starting with the

answer number being processed when the limit was reached. To begin Each SELECT E-number list with E1, enter SET SELECT RENUMBER at an arrow prompt (=>). Each subsequent SELECT command erases the previously created E-numbers and starts with E1. Enter HELP SET SELECT for more information.

To analyze extracted terms, use the ANALYZE command. See HELP ANALYZE for more information.

```
=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    41.90     108.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -4.20      -7.00

FILE 'CAPLUS' ENTERED AT 08:14:50 ON 27 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 27 Sep 2004  VOL 141 ISS 14
FILE LAST UPDATED: 26 Sep 2004  (20040926/ED)
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> pharmaceutical s;ts
        190133 PHARMACEUTICAL
         84688 PHARMACEUTICALS
        241236 PHARMACEUTICAL
                  (PHARMACEUTICAL OR PHARMACEUTICALS)
       2595533 S
L28          46 PHARMACEUTICAL S
                  (PHARMACEUTICAL(W)S)


         22026 TS
           258 TSES
L29      22284 TS
                  (TS OR TSES)

=> logoff hold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    15.14     123.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
```

```
                                                          ENTRY     SESSION
CA SUBSCRIBER PRICE                                        0.00       -7.00

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:28:01 ON 27 SEP 2004

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 08:54:40 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 08:54:40 ON 27 SEP 2004
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY     SESSION
FULL ESTIMATED COST                                      15.14     123.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY     SESSION
CA SUBSCRIBER PRICE                                       0.00      -7.00

=> d his

     (FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 07:15:56 ON 27 SEP 2004
               E COMBRETASTATIN A-4/CN
L1             1 E9
L2             1 E10

     FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3            54 L1
L4            41 L2
L5            92 L3 OR L4
L6        410638 NUCLEOTIDE
L7             4 L5 AND L6
L8        281040 LITHIUM
L9             3 L5 AND L8
L10            8 L1/PREP

     FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
               DEL ALKYLATIN/L
               DEL ESTERODOR/L
               DEL GABACOMPDS/A
               DEL GORDSRCH/L
               DEL INDIUMCL3/A
               DEL LTWENTAUGFOR/A
               DEL NEOTAMECRYST/A
               DEL NVLARMFULGEN/A
               DEL POHBENZALDEH/A
               DEL PROSTACMPD15/A
               DEL STILLEAPP/L

     FILE 'REGISTRY' ENTERED AT 07:46:20 ON 27 SEP 2004
               E TETRABROMOMETHANE/CN
```

```
L11             1 E3
                  E TETRACHLOROMOMETHANE/CN
                  E TETRACHLOROMETHANE/CN
L12             1 E3
                  E TETRAIODOMETHANE/CN
L13             1 E3

     FILE 'CAPLUS' ENTERED AT 07:48:31 ON 27 SEP 2004
L14          2953 L11
L15         40657 L12
L16           325 L13
L17         42754 L14 OR L15 OR L16
L18         39583 ?PHOSPHITE
L19           207 L17 AND L18
L20           207 L17 AND L18
L21            52 L17(L)L18
L22             4 COMBRESTATIN
L23           437 COMBRETASTATIN
L24             0 L21 AND L23
L25            19 L23 AND L18
L26           207 L17 AND L19
L27            19 L18 AND L23

     FILE 'CAPLUS' ENTERED AT 08:14:50 ON 27 SEP 2004
L28            46 PHARMACEUTICAL S
L29         22284 TS

=> pharmaceutical salt
          190133 PHARMACEUTICAL
           84688 PHARMACEUTICALS
          241236 PHARMACEUTICAL
                   (PHARMACEUTICAL OR PHARMACEUTICALS)
          721367 SALT
          563198 SALTS
         1075868 SALT
                   (SALT OR SALTS)
L30          157 PHARMACEUTICAL SALT
                   (PHARMACEUTICAL(W)SALT)

=> review
         1925703 REVIEW
           65110 REVIEWS
L31      1955208 REVIEW
                   (REVIEW OR REVIEWS)

=> l30 and l31
L32            3 L30 AND L31

=> d l32 1-3 ti

L32  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Pharmaceutical salts

L32  ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Salt selection for basic drugs

L32  ANSWER 3 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Pharmaceutical salts


=> d l32 1-3 ti fbib abs

L32  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
```

TI **Pharmaceutical salts**
AN 2000:716588 CAPLUS
DN 134:357426
TI **Pharmaceutical salts**
AU Neau, Steven H.
CS University of Missouri-Kansas City School of Pharmacy, Kansas City, MO, USA
SO Water-Insoluble Drug Formulation (2000), 405-425. Editor(s): Liu, Rong. Publisher: Interpharm Press, Buffalo Grove, Ill.
CODEN: 69AMSN
DT Conference; General Review
LA English
AB A **review** with 65 refs. Topics discussed include classical salts, organic salts, polymeric and macromol. salts; predictability of solubility, formulation considerations, and salt selection process.
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
TI Salt selection for basic drugs
AN 1987:38282 CAPLUS
DN 106:38282
TI Salt selection for basic drugs
AU Gould, Philip L.
CS Pharm. Res. Dev. Dep., Pfizer Cent. Res., Sandwich/Kent, UK
SO International Journal of Pharmaceutics (1986), 33(1-3), 201-17
CODEN: IJPHDE; ISSN: 0378-5173
DT Journal; General Review
LA English
AB A **review** discussion with 23 refs. on the approaches for providing rationale to salt selection for basic drugs. Desired characteristics of the salt form, given sufficient strength and toxicol. suitability of the conjugate acid, are discussed on the basis of physicochem. properties.

L32 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
TI **Pharmaceutical salts**
AN 1977:60441 CAPLUS
DN 86:60441
TI **Pharmaceutical salts**
AU Berge, Stephen M.; Bighley, Lyle D.; Monkhouse, Donald C.
CS Cent. Res., Pfizer Inc., Groton, CT, USA
SO Journal of Pharmaceutical Sciences (1977), 66(1), 1-19
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal; General Review
LA English
AB A **review** with 294 refs. on the general pharmacy, physicochem. properties, bioavailability, pharmaceutical properties, and toxicol. of **pharmaceutical salts**.

=>
=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	42.82	151.62
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-9.10

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 09:13:07 ON 27 SEP 2004

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 09:25:12 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 09:25:12 ON 27 SEP 2004
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	42.82	151.62

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-9.10

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	42.82	151.62

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-9.10

FILE 'CAPLUS' ENTERED AT 09:25:19 ON 27 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 27 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 26 Sep 2004 (20040926/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.44	152.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-9.10

FILE 'REGISTRY' ENTERED AT 09:25:28 ON 27 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 SEP 2004 HIGHEST RN 751457-34-8
DICTIONARY FILE UPDATES: 24 SEP 2004 HIGHEST RN 751457-34-8

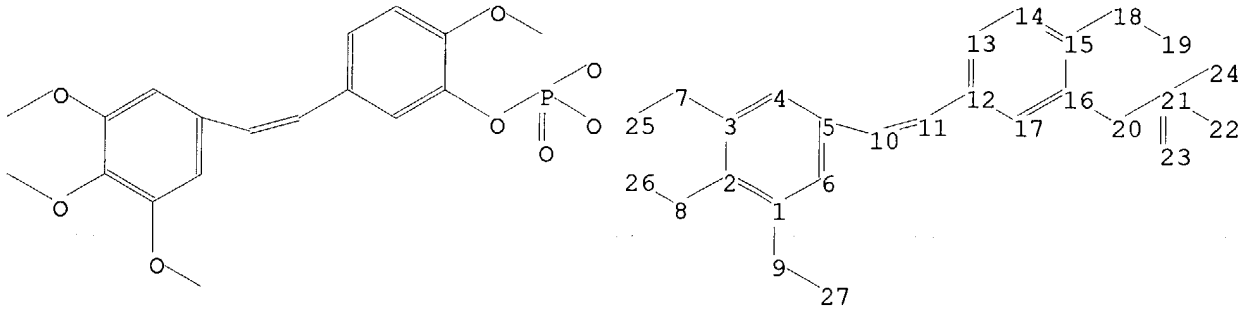
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Examination Auxillary files\09582950\09582950 compound (III) fixed H.str



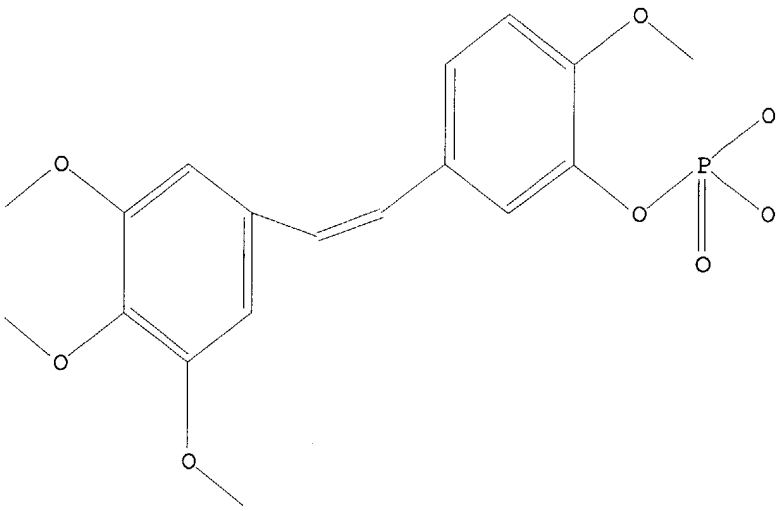
chain nodes :
7 8 9 10 11 18 19 20 21 22 23 24 25 26 27
ring nodes :
1 2 3 4 5 6 12 13 14 15 16 17
chain bonds :
1-9 2-8 3-7 5-10 7-25 8-26 9-27 10-11 11-12 15-18 16-20 18-19 20-21 21-22 21-23 21-24
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17
exact/norm bonds :
1-9 2-8 3-7 7-25 8-26 9-27 15-18 16-20 18-19 20-21 21-22 21-23 21-24
exact bonds :
5-10 10-11 11-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

Hydrogen count :
13:>= minimum 1 14:>= minimum 1 17:>= minimum 1

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS

L33 STRUCTURE UPLOADED

=> d l33
L33 HAS NO ANSWERS
L33 STR



Structure attributes must be viewed using STN Express query preparation.

=> search l33 sss sam
SAMPLE SEARCH INITIATED 09:25:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 7 TO 298
PROJECTED ANSWERS: 2 TO 124

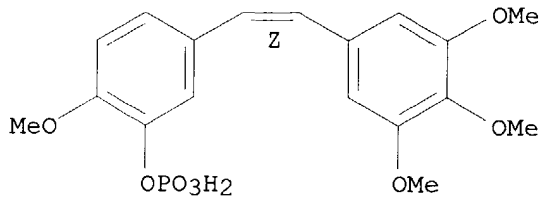
L34 2 SEA SSS SAM L33

=> d scan

L34 2 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Phenol, 2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-, dihydrogen phosphate, manganese salt (9CI)
MF C18 H21 O8 P . Mn

CM 1

Double bond geometry as shown.



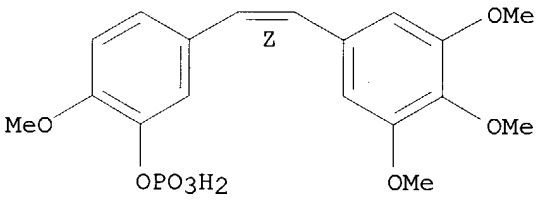
CM 2

Mn

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L34 2 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Phenol, 2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-, dihydrogen phosphate (9CI)
MF C18 H21 O8 P
CI COM

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> search l33 sss full
FULL SEARCH INITIATED 09:26:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 145 TO ITERATE

100.0% PROCESSED 145 ITERATIONS 50 ANSWERS
SEARCH TIME: 00.00.01

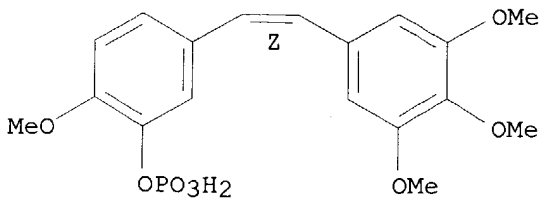
L35 50 SEA SSS FUL L33

=> d scan

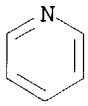
L35 50 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Phenol, 2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-, dihydrogen phosphate, compd. with pyridine (1:1) (9CI)
MF C18 H21 O8 P . C5 H5 N

CM 1

Double bond geometry as shown.



CM 2



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.84	307.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.10

FILE 'CAPLUS' ENTERED AT 09:26:37 ON 27 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 26 Sep 2004 (20040926/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> l35
L36 98 L35

=> d l36 88-98 ti

L36 ANSWER 88 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Determination of combretastatin A-4 and its drug in plasma by high-performance liquid chromatography

L36 ANSWER 89 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Targeting the tumor vasculature with combretastatin A-4 disodium phosphate: effects on radiation therapy

L36 ANSWER 90 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI The effect of combretastatin A-4 disodium phosphate in a C3H mouse mammary carcinoma and a variety of murine spontaneous tumors

L36 ANSWER 91 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Effects of combretastatin on murine tumors monitored by 31P MRS, 1H MRS and 1H MRI

L36 ANSWER 92 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents. 389. New syntheses of the combretastatin A-4 prodrug

L36 ANSWER 93 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate

L36 ANSWER 94 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Combretastatin A-4, an agent that displays potent and selective toxicity toward tumor vasculature

L36 ANSWER 95 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Combretastatin A-4 prodrug

L36 ANSWER 96 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis of water-soluble prodrugs of the cytotoxic agent combretastatin A4

L36 ANSWER 97 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs

L36 ANSWER 98 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of combretastatin A4 analogs as neoplasm inhibitors

=> l35/prep
98 L35
3201185 PREP/RL
L37 15 L35/PREP
(L35 (L) PREP/RL)

=> ?phosphite
L38 39583 ?PHOSPHITE

=> l37 and l38
L39 6 L37 AND L38

=> d l39 1-6 ti

L39 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of resveratrol and sodium resverastatin phosphate derivatives for use in pharmaceutical compositions as antineoplastic and antimicrobial agents

L39 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods of synthesizing prodrugs of combretastatin A-4

L39 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of combretastatin A4 prodrugs and their trans-isomers for use as antitumor agents

L39 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 393. Synthesis of the trans-isomer of combretastatin A-4 prodrug

L39 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents. 389. New syntheses of the combretastatin A-4 prodrug

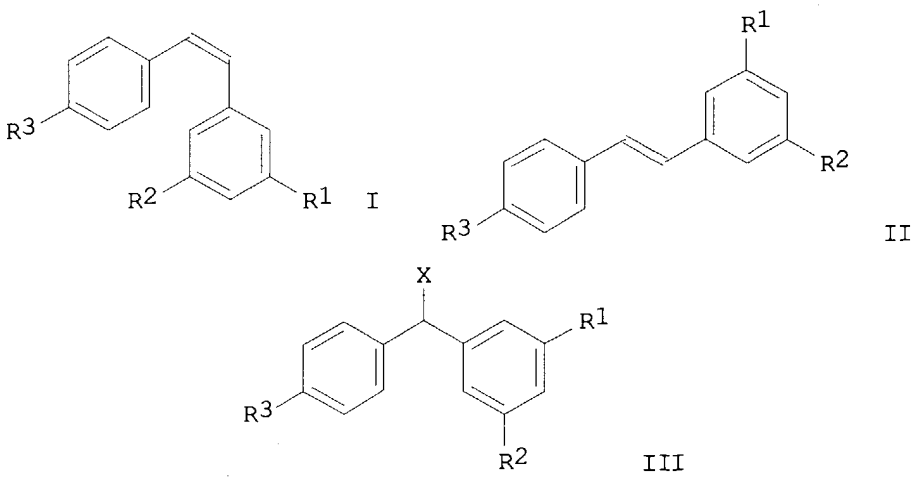
L39 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate

=> d l39 1-3 ti fbib abs

L39 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of resveratrol and sodium resverastatin phosphate derivatives for use in pharmaceutical compositions as antineoplastic and antimicrobial agents
AN 2003:836866 CAPLUS
DN 139:337828
TI Preparation of resveratrol and sodium resverastatin phosphate derivatives for use in pharmaceutical compositions as antineoplastic and antimicrobial agents
IN Pettit, George R.; Grealish, Matthew P.
PA Arizona Board of Regents, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003086414	A1	20031023	WO 2003-US11008	20030410
W: CA, JP, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
			US 2002-371782P	P 20020410

OS CASREACT 139:337828
GI



AB Combretastatin A-4, resveratrol, resverastatin, benzophenone and benzhydrol derivs. and analogs, such as I, II and III [R1, R2, R3 = OH,

OMe; X = :O, OH], were prepared for therapeutic uses as antineoplastic and antimicrobial agents. Thus, (E)- and (Z)-3,5,4'-trimethoxystilbene were prepared in 91% overall yield via an olefination reaction of 4-methoxybenzyltriphenylphosphonium bromide and 3,5-dimethoxybenzaldehyde using BuLi in THF. The prepared compds. were assayed for inhibition of tubulin polymerization and colchicine binding and for activity against cancer cell lines, such as P388 leukemia and pancreas-a BXPC-3, and for activity against organisms, such as S. aureus, C. albicans and E. coli.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods of synthesizing prodrugs of combretastatin A-4
AN 2002:72094 CAPLUS
DN 136:134622
TI Methods of synthesizing prodrugs of combretastatin A-4
IN Seyedi, Faye; Gale, Jonathan; Haider, Reem; Hoare, John
PA Oxigene, Inc., USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006279	A1	20020124	WO 2001-US22403	20010717
	WO 2002006279	C1	20020418		
	WO 2002006279	C2	20030403		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

				US 2000-218766P	P 20000717
	US 2002119951	A1	20020829	US 2001-908321	20010717
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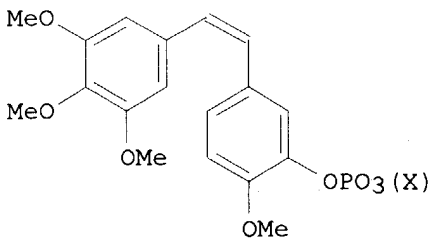
OS CASREACT 136:134622
GI



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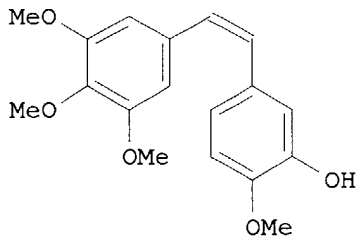

II

AB The present invention discloses improved methods of synthesizing a phosphate ester of combretastatin A-4, such as I [X = HZ1, Z2; Z1 = Na+, Li+; Z2 = Mg+2, Zn+2, Ca+2, Cs+2, imidazole, morpholine, etc.], and trans-isomers thereof. Thus, combretastatin A-4 (II) is reacted with **dibenzylphosphite** in the presence of carbon tetrabromide, or with 2,2,2-trichloroethyl phosphorodichloridate, to form a phosphate ester of combretastatin A-4 with protecting groups thereon.

L39 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of combretastatin A4 prodrugs and their trans-isomers for use as antitumor agents
AN 1999:451301 CAPLUS
DN 131:73507
TI Preparation and formulation of combretastatin A4 prodrugs and their trans-isomers for use as antitumor agents
IN Pettit, George R.; Rhodes, Monte R.
PA Arizona State University, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
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				US 1998-111531P	P	19981209
	CA 2314238	AA	19990715	CA 1999-2314238		19990108
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				US 1998-111531P	P	19981209
				WO 1999-US419	W	19990108
	EP 1045853	A1	20001025	EP 1999-902121		19990108
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				US 1998-111531P	P	19981209
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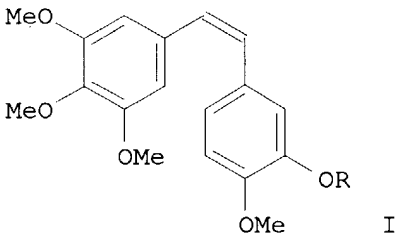

I

AB Combretastatin A4 I (R = H) and analogous phosphate prodrugs I [R = PO(OR1)OR2; R1, R2 = H, Na, Ca, Cs, Li, Mg, Mn, Zn, imidazole, morpholine, piperazine piperidine, pyrazole, pyridine, adenosine, cinchonine, glucosamine quinine, quinidine, tetracycline, verapamil; R1 = R2 = H, benzyl] and (E)-Combretastatin A4 phosphate analogs were prepared and formulated for use as water soluble antineoplastic agents. Thus, combretastatin A4 was reacted with dibenzyl **phosphite** to give dibenzyl ester I [R = P(O)(OCH2Ph)2] in 98% yield. Also, combretastatin A4 was converted to the sodium phosphate salt I [R = PO3HNa] via the formation of the silylethyl ester I [R = P(O)(OCH2CH2SiMe3)2]. The combretastatin A4 phosphate esters were tested for antitumor activity against a variety of cancer cell lines and were also tested for antimicrobial activity against bacterial and fungal strains.

```
RE.CNT  3      THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> logoff hold
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        21.40     329.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -2.10     -11.20

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 09:33:13 ON 27 SEP 2004

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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FULL ESTIMATED COST                                        21.40     329.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                        -2.10     -11.20

=> d his

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L2             1 E10

     FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3            54 L1
L4            41 L2
L5            92 L3 OR L4
L6        410638 NUCLEOTIDE
L7             4 L5 AND L6
L8        281040 LITHIUM
L9             3 L5 AND L8
L10            8 L1/PREP

     FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
               DEL ALKYLATIN/L
               DEL ESTERODOR/L
               DEL GABACOMPDS/A
               DEL GORDSRCH/L
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                DEL INDIUMCL3/A
                DEL LTWENTAUGFOR/A
                DEL NEOTAMECRYST/A
                DEL NVLARMFULGEN/A
                DEL POHBENZALDEH/A
                DEL PROSTACMPD15/A
                DEL STILLEAPP/L

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L11           1 E3
                E TETRACHLOROMOMETHANE/CN
                E TETRACHLOROMETHANE/CN
L12           1 E3
                E TETRAIODOMETHANE/CN
L13           1 E3

     FILE 'CAPLUS' ENTERED AT 07:48:31 ON 27 SEP 2004
L14        2953 L11
L15       40657 L12
L16         325 L13
L17       42754 L14 OR L15 OR L16
L18       39583 ?PHOSPHITE
L19         207 L17 AND L18
L20         207 L17 AND L18
L21          52 L17(L)L18
L22           4 COMBRESTATIN
L23         437 COMBRETASTATIN
L24           0 L21 AND L23
L25          19 L23 AND L18
L26         207 L17 AND L19
L27          19 L18 AND L23

     FILE 'CAPLUS' ENTERED AT 08:14:50 ON 27 SEP 2004
L28          46 PHARMACEUTICAL S
L29       22284 TS
L30         157 PHARMACEUTICAL SALT
L31     1955208 REVIEW
L32           3 L30 AND L31

     FILE 'CAPLUS' ENTERED AT 09:25:19 ON 27 SEP 2004

     FILE 'REGISTRY' ENTERED AT 09:25:28 ON 27 SEP 2004
L33             STRUCTURE UPLOADED
L34           2 SEARCH L33 SSS SAM
L35          50 SEARCH L33 SSS FULL

     FILE 'CAPLUS' ENTERED AT 09:26:37 ON 27 SEP 2004
L36          98 L35
L37          15 L35/PREP
L38       39583 ?PHOSPHITE
L39           6 L37 AND L38

=> nuclotide
            19 NUCLOTIDE
             8 NUCLOTIDES
L40         27 NUCLOTIDE
                (NUCLOTIDE OR NUCLOTIDES)

=> nucleotide
        358966 NUCLEOTIDE
        107591 NUCLEOTIDES
L41     410638 NUCLEOTIDE
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(NUCLEOTIDE OR NUCLEOTIDES)

=> l41 and l23
L42 29 L41 AND L23

=> l41(l)l23
L43 1 L41(L)L23

=> d l43 ti fbib abs

L43 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
TI Effects of combretastatin on murine tumors monitored by 31P MRS, 1H MRS and 1H MRI
AN 1999:5891 CAPLUS
DN 130:204769
TI Effects of combretastatin on murine tumors monitored by 31P MRS, 1H MRS and 1H MRI
AU Maxwell, R. J.; Pharm, B.; Nielsen, F. U.; Breidahl, T.; Stodkilde-Jorgensen, H.; Horsman, M. R.
CS Gray Laboratory Cancer Research Trust, Northwood, HA6 2JR, UK
SO International Journal of Radiation Oncology, Biology, Physics (1998), 42(4), 891-894
CODEN: IOBPD3; ISSN: 0360-3016
PB Elsevier Science Inc.
DT Journal
LA English
AB **Combretastatins** have tubulin-binding activity and are being investigated for their toxicity against tumor vasculature. We report the use of 31P and 1H magnetic resonance (MR) spectroscopy and 1H MR imaging for monitoring the effects of **combretastatin** A-4 prodrug (100mg/kg, i.p.) on energy metabolism and necrosis, resp., in the C3H murine mammary tumor. The tumors (volume ca. 200mm3) were grown in the hind foot of mice. MR examns. were performed without anesthesia within a 7.1 T magnet. 31P MRS (TR = 6 s) was performed before treatment and at 1-, 2-, 3-, and 24-h after injection of drug or saline via an i.p. line. 1H MRS (PRESS; 24μl voxel; TR = 2 s; TE = 135 ms) and both T1-weighted (TR = 0.2 s; TE = 0.02 s) and T2-weighted (TR = 2 s; TE = 0.20 s) 1H MRI were performed before treatment and 2.5 and 24 h afterwards. The ratio β-**nucleotide** triphosphate/inorg. phosphate fell by 33% within 1 h of treatment and remained constant for a further 2 h. A small but significant fall in pH (by 0.11 units) was observed at 1 h. Although an increase in the 1H MR spectroscopy signal at about 1.32 ppm (predominantly from lactate) was observed in some tumors following **combretastatin** treatment, this effect was not seen consistently. No changes in the intensity of T2-weighted 1H MR images or in tumor necrosis (measured histol.) were detected within 3 h of treatment. The reduction in tumor energetics and pH was consistent with a reduction in tumor blood flow but this occurred before any significant incidence of haemorrhagic necrosis was detected. The **combretastatin** dose used to achieve these effects was less than one tenth of the maximum tolerated dose in mice.
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l43 20-29 ti
1 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):end

=> d l42 20-29 ti

L42 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of thienopyrimidines as mitotic kinesin inhibitors for the

treatment of cancer

L42 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of thiazolopyrimidinones as mitotic kinesin inhibitors for treatment of cancer

L42 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of cyclopenta[d]pyrimidinones as mitotic kinesin inhibitors for the treatment of cancer

L42 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Anti-CD30 antibody-cytotoxic agent conjugates for treating non-cancer immunological disorders

L42 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of quinazolinone mitotic kinesin inhibitors for treating cancer

L42 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods for evaluating treatment efficacy on Kaposi's Sarcoma using angiogenesis associated gene marker

L42 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Conjugates activated by cell surface proteases and therapeutic uses thereof

L42 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI RT-PCR based methods for determining cancer treatment efficacy using expression profiles of marker genes

L42 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Compositions and methods for cancer treatment by selectively inhibiting VEGF

L42 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
TI Effects of **combretastatin** on murine tumors monitored by 31P MRS, 1H MRS and 1H MRI

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	33.33	341.23
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.80	-11.90

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:02:39 ON 27 SEP 2004

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Welcome to STN International! Enter x:x

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PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 10:16:49 ON 27 SEP 2004

FILE 'CAPLUS' ENTERED AT 10:16:49 ON 27 SEP 2004
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FULL ESTIMATED COST	33.33	341.23

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.80	-11.90

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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CA SUBSCRIBER PRICE	-2.80	-11.90

FILE 'REGISTRY' ENTERED AT 10:17:01 ON 27 SEP 2004
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STRUCTURE FILE UPDATES: 24 SEP 2004 HIGHEST RN 751457-34-8
DICTIONARY FILE UPDATES: 24 SEP 2004 HIGHEST RN 751457-34-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e dibenzylphosphite/cn

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E5	1	DIBENZYLPHOSPHORYL CHLORIDE/CN
E6	1	DIBENZYLPROPYLPHOSPHINE OXIDE/CN
E7	1	DIBENZYLPYRUVIC ACID/CN
E8	1	DIBENZYLRUBEANIC ACID/CN
E9	1	DIBENZYLSELENIUM OXIDE/CN
E10	1	DIBENZYLSELENONIUM CYANO(METHOXYCARBONYL)METHYLIDE/CN
E11	1	DIBENZYLSELENONIUM DICYANOMETHYLIDE/CN
E12	1	DIBENZYLSILANE/CN

=> e dibenzyl phosphite/cn

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E3	1 -->	DIBENZYL PHOSPHITE/CN
E4	1	DIBENZYL PHOSPHONATE/CN
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E12           1     DIBENZYL PROPYLMALONATE/CN

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L44           1 "DIBENZYL PHOSPHITE"/CN

=> d l44

L44  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   17176-77-1  REGISTRY
CN   Phosphonic acid, bis(phenylmethyl) ester (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Benzyl phosphonate ((C7H7O)2HPO) (6CI, 7CI)
CN   Phosphonic acid, dibenzyl ester (8CI)
OTHER NAMES:
CN   Dibenzyl hydrogen phosphite
CN   Dibenzyl phosphite
CN   Dibenzyl phosphonate
AR   538-60-3
FS   3D CONCORD
MF   C14 H15 O3 P
CI   COM
LC   STN Files:   ADISNEWS, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS,
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       IFICDB, IFIPAT, IFIUDB, MRCK*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); RACT
       (Reactant or reagent); USES (Uses); NORL (No role in record)
RL.NP  Roles from non-patents:  BIOL (Biological study); FORM (Formation,
       nonpreparative); PREP (Preparation); PROC (Process); RACT (Reactant or
       reagent); NORL (No role in record)
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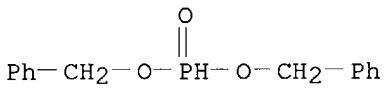

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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             259 REFERENCES IN FILE CAPLUS (1907 TO DATE)
               2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


=> file caplus
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FULL ESTIMATED COST                                       6.62     347.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                       0.00     -11.90
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FILE COVERS 1907 - 27 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 26 Sep 2004 (20040926/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

FILE 'REGISTRY' ENTERED AT 07:15:56 ON 27 SEP 2004
E COMBRETASTATIN A-4/CN
L1 1 E9
L2 1 E10

FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3 54 L1
L4 41 L2
L5 92 L3 OR L4
L6 410638 NUCLEOTIDE
L7 4 L5 AND L6
L8 281040 LITHIUM
L9 3 L5 AND L8
L10 8 L1/PREP

FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
DEL ALKYLATIN/L
DEL ESTERODOR/L
DEL GABACOMPDS/A
DEL GORDSRCH/L
DEL INDIUMCL3/A
DEL LTWENTAUGFOR/A
DEL NEOTAMECRYST/A
DEL NVLARMFULGEN/A
DEL POHBENZALDEH/A
DEL PROSTACMPD15/A
DEL STILLEAPP/L

FILE 'REGISTRY' ENTERED AT 07:46:20 ON 27 SEP 2004
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E TETRACHLOROMOMETHANE/CN
E TETRACHLOROMETHANE/CN
L12 1 E3
E TETRAIODOMETHANE/CN
L13 1 E3

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L14         2953 L11
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L16          325 L13
L17        42754 L14 OR L15 OR L16
L18        39583 ?PHOSPHITE
L19          207 L17 AND L18
L20          207 L17 AND L18
L21           52 L17(L)L18
L22            4 COMBRESTATIN
L23          437 COMBRETASTATIN
L24            0 L21 AND L23
L25           19 L23 AND L18
L26          207 L17 AND L19
L27           19 L18 AND L23

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L29        22284 TS
L30          157 PHARMACEUTICAL SALT
L31      1955208 REVIEW
L32            3 L30 AND L31

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     FILE 'REGISTRY' ENTERED AT 09:25:28 ON 27 SEP 2004
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L35           50 SEARCH L33 SSS FULL

     FILE 'CAPLUS' ENTERED AT 09:26:37 ON 27 SEP 2004
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L37           15 L35/PREP
L38        39583 ?PHOSPHITE
L39            6 L37 AND L38
L40           27 NUCLOTIDE
L41       410638 NUCLEOTIDE
L42           29 L41 AND L23
L43            1 L41(L)L23

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                E DIBENZYL PHOSPHITE/CN
L44            1 E3

     FILE 'CAPLUS' ENTERED AT 10:17:51 ON 27 SEP 2004

=> l44 and l17
           271 L44
L45            3 L44 AND L17

=> d l45 1-3 ti fbib abs

L45  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Methods of synthesizing prodrugs of combretastatin A-4
AN   2002:72094  CAPLUS
DN   136:134622
TI   Methods of synthesizing prodrugs of combretastatin A-4
IN   Seyedi, Faye; Gale, Jonathan; Haider, Reem; Hoare, John
PA   Oxigene, Inc., USA
SO   PCT Int. Appl., 41 pp.
     CODEN: PIXXD2
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DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002006279	A1	20020124	WO 2001-US22403	20010717
WO 2002006279	C1	20020418		
WO 2002006279	C2	20030403		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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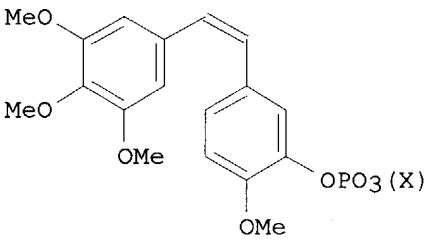
US 2002119951	A1	20020829	US 2001-908321	20010717
US 6743937	B2	20040601		
			US 2000-218766P	P 20000717

OS CASREACT 136:134622
GI



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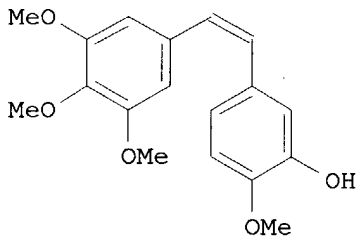

II

AB The present invention discloses improved methods of synthesizing a phosphate ester of combretastatin A-4, such as I [X = HZ1, Z2; Z1 = Na+, Li+; Z2 = Mg+2, Zn+2, Ca+2, Cs+2, imidazole, morpholine, etc.], and trans-isomers thereof. Thus, combretastatin A-4 (II) is reacted with dibenzylphosphite in the presence of carbon tetrabromide, or with 2,2,2-trichloroethyl phosphorodichloridate, to form a phosphate ester of combretastatin A-4 with protecting groups thereon.

L45 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
TI Organophosphorus esters. VIII. Phase-transfer-catalyzed phosphorylation of amines in an aqueous system
AN 1975:563742 CAPLUS
DN 83:163742
TI Organophosphorus esters. VIII. Phase-transfer-catalyzed phosphorylation of amines in an aqueous system
AU Zwierzak, A.
CS Inst. Org. Chem., Tech. Univ. Lodz, Lodz, Pol.
SO Synthesis (1975), (8), 507-9
CODEN: SYNTBF; ISSN: 0039-7881
DT Journal
LA English
AB Phosphorylation by (R1O)2P(O)H (R1 = Et, benzyl, Me3C) of R2R3NH (R2 = H, Et; R3 = Ph, cyclohexyl, benzyl, Et) by the Atherton-Todd method was accomplished in a 2-phase system in the presence of 5 mol.% Et3N+CH2Ph Cl-, yields were 35-93% and 3 different procedures were given.

L45 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

TI Phosphorylation. III. Further observations on the reaction of phosphites with polyhalogen compounds in the presence of bases and its application to the phosphorylation of alcohols
AN 1947:32643 CAPLUS
DN 41:32643
OREF 41:6544d-h
TI Phosphorylation. III. Further observations on the reaction of phosphites with polyhalogen compounds in the presence of bases and its application to the phosphorylation of alcohols
AU Atherton, F. R.; Todd, A. R.
CS Univ. of Cambridge, UK
SO Journal of the Chemical Society, Abstracts (1947) 674-8
CODEN: JCSAAZ; ISSN: 0590-9791
DT Journal
LA Unavailable
OS CASREACT 41:32643
AB cf. C.A. 40, 1801.7. In a further study of the reaction of (PhCH2O)2POH (I) with CCl4 in the presence of bases, it has been found that the following compds. are active: ClCH2CCl3, ClF2CCCl3, ClCH2CFCl2, ClF2CCFCl2, (Cl2FC)2, Cl3CCCl2CCl3, (Cl3CCCl2)2, and Cl2C:CClCCl3. None of these compds. showed any practical advantage over CCl4. With 0.01 mol. I and 0.005-0.015 mol. of a halogen compound (CH2Cl2 as diluent), the following yields of (PhCH2O)2PONH2 or dibenzyl (cyclohexylamino) phosphonate were obtained: CHI3 81, 83%; CHBr3 90, 80%; CHBrCl2 43, 87%; (CCl2Br)2 91, 90%; CBr4 -, 84%. The yield of anilinophosphonate with CBr4 was: I 91%, (EtO)2POH 88%, (iso-PrO)2POH 40%. On passage of a slow stream of NH3 through equimol. quantities of (iso-PrO)2POH and the halogen compound in ether, (CCl3)2 gives 70% (Cl2C:)2, CHI3 80% CH2I2, CBr4 59% CH2Br2, and (CCl2Br)2 54% (Cl2C:)2 and 6.5% Cl2C:CClBr. The most suitable compound appears to be CBrCl3, prepared in 74% yield by passage of 400 cc. CHCl3 and 320 g. Br in a N stream through a vertical SiO2 tube at 250°. By its use the following were prepared: (EtO)2PONHPh, 88%; (iso-PrO)2PONHPh, 62%; (PhCH2O)2PONHPh, 92%; dibenzyl (2-naphthylamino) phosphonate, m. 75.5-6.5°, 93%; p-toluidino analog, m. 89.5-90.5°, 89%, N-methylanilino analog, m. 86-7°, 64%. I (5.24 g.), 3 cc. EtOH, 5 cc. 2,6-lutidine, 5 cc. CBrCl3, and 25 cc. ether, kept at room temperature 2.5 hrs., give 51% Ba Et phosphate. (PhO)2POH (2.34 g.) in 25 cc. CCl4, treated with NH3 15 min., gives 82% (PhO)2PONH2. Tetrabenzyl pyrophosphate can be prepared in 61% yield. The mechanism of the reaction is considered in the light of these further studies and it is concluded that, contrary to the earlier views, the main pathway of the reaction involves intermediate formation of a halophosphonate which then acts as a phosphorylating agent.

=> atherton
L46 258 ATHERTON

=> l23 and l46
L47 0 L23 AND L46

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.55	360.40
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-14.00

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:21:49 ON 27 SEP 2004

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 10:51:09 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 10:51:09 ON 27 SEP 2004
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.55	360.40

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-14.00

=> save temp all combretsrch/l
L# LIST L1-L47 HAS BEEN SAVED AS 'COMBRETSRCH/L'

=>
=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	23.99	371.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-14.00

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:06:49 ON 27 SEP 2004

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 11:49:49 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 11:49:49 ON 27 SEP 2004
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	23.99	371.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-14.00

=> logoff hold

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        23.99     371.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -2.10     -14.00

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:49:57 ON 27 SEP 2004

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:
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SESSION RESUMED IN FILE 'CAPLUS' AT 11:56:22 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 11:56:22 ON 27 SEP 2004
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        23.99     371.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -2.10     -14.00

=> d his

     (FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 07:15:56 ON 27 SEP 2004
                E COMBRETASTATIN A-4/CN
L1              1 E9
L2              1 E10

     FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3             54 L1
L4             41 L2
L5             92 L3 OR L4
L6         410638 NUCLEOTIDE
L7              4 L5 AND L6
L8         281040 LITHIUM
L9              3 L5 AND L8
L10             8 L1/PREP

     FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
                DEL ALKYLATIN/L
                DEL ESTERODOR/L
                DEL GABACOMPDS/A
                DEL GORDSRCH/L
                DEL INDIUMCL3/A
                DEL LTWENTAUGFOR/A
                DEL NEOTAMECRYST/A
                DEL NVLARMFULGEN/A
                DEL POHBENZALDEH/A
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                DEL PROSTACMPD15/A
                DEL STILLEAPP/L

      FILE 'REGISTRY' ENTERED AT 07:46:20 ON 27 SEP 2004
                E TETRABROMOMETHANE/CN
L11             1 E3
                E TETRACHLOROMOMETHANE/CN
                E TETRACHLOROMETHANE/CN
L12             1 E3
                E TETRAIODOMETHANE/CN
L13             1 E3

      FILE 'CAPLUS' ENTERED AT 07:48:31 ON 27 SEP 2004
L14          2953 L11
L15         40657 L12
L16           325 L13
L17         42754 L14 OR L15 OR L16
L18         39583 ?PHOSPHITE
L19           207 L17 AND L18
L20           207 L17 AND L18
L21            52 L17(L)L18
L22             4 COMBRESTATIN
L23           437 COMBRETASTATIN
L24             0 L21 AND L23
L25            19 L23 AND L18
L26           207 L17 AND L19
L27            19 L18 AND L23

      FILE 'CAPLUS' ENTERED AT 08:14:50 ON 27 SEP 2004
L28            46 PHARMACEUTICAL S
L29         22284 TS
L30           157 PHARMACEUTICAL SALT
L31       1955208 REVIEW
L32             3 L30 AND L31

      FILE 'CAPLUS' ENTERED AT 09:25:19 ON 27 SEP 2004

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L33               STRUCTURE UPLOADED
L34             2 SEARCH L33 SSS SAM
L35            50 SEARCH L33 SSS FULL

      FILE 'CAPLUS' ENTERED AT 09:26:37 ON 27 SEP 2004
L36            98 L35
L37            15 L35/PREP
L38         39583 ?PHOSPHITE
L39             6 L37 AND L38
L40            27 NUCLOTIDE
L41        410638 NUCLEOTIDE
L42            29 L41 AND L23
L43             1 L41(L)L23

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L44             1 E3

      FILE 'CAPLUS' ENTERED AT 10:17:51 ON 27 SEP 2004
L45             3 L44 AND L17
L46           258 ATHERTON
L47             0 L23 AND L46
                SAVE TEMP ALL COMBRETSRCH/L
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=> d l37 10-15 ti

L37 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents. 389. New syntheses of the combretastatin A-4 prodrug

L37 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic Agents. 379. Synthesis of Phenstatin Phosphate

L37 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Combretastatin A-4 prodrug

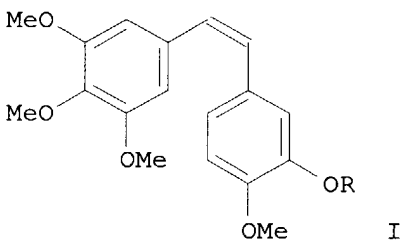
L37 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis of water-soluble prodrugs of the cytotoxic agent combretastatin A4

L37 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs

L37 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of combretastatin A4 analogs as neoplasm inhibitors

=> d l37 14,15 ti fbib abs

L37 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs
AN 1995:661775 CAPLUS
DN 123:227731
TI Antineoplastic agents. 322. Synthesis of combretastatin A-4 prodrugs
AU Pettit, George R.; Temple, Carroll, Jr.; Narayanan, Ven L.; Varma, Ravi; Simpson, Michael J.; Boyd, Michael R.; Rener, Gregory A.; Bansal, Namita
CS Cancer Research Institute and Department of Chemistry, Arizona State University, Temple, AZ, 85287-1604, USA
SO Anti-Cancer Drug Design (1995), 10(4), 299-309
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal
LA English
GI



I

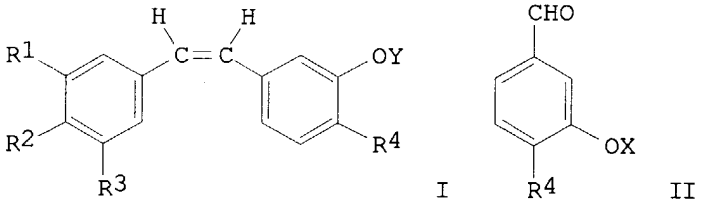
AB Combretastatin A-4 (I, R = H), the principal cancer cell growth-inhibitory constituent of the Zulu medicinal plant (Combretum caffrum, has been undergoing preclin. development. However, the very limited water solubility of this phenol has complicated drug formation. Hence, derivs. of the combretastatin A-4 3'-phenol group were prepared for evaluation as possible water-soluble prodrugs. As observed for combretastatin A-4, the sodium salt (I,
R = Na), potassium salt (I, R = K), and hemisuccinic acid ester (I, R = COCH2CH2CO2H) derivs. were essentially insol. in water. Indeed, these substances regenerated combretastatin A-4 upon reaction with water. A

series of other simple derivs., e.g. I [R = COCH(NH2)CH2CH2CO2H], proved unsatisfactory in terms of water solubility or stability, or both. The most soluble derivs. evaluated included the ammonium [I, R = P(O)(OH)ONH4], and potassium [I, R = P(O)(OK)2] and sodium [I, R = P(O)(ONa)2] phosphate salts, where the latter two proved most stable and suitable. Both the potassium and sodium phosphate derivs. of combretastatin A-4 were also found to exhibit the requisite biol. properties necessary for a useful prodrug. The sodium phosphate salt was selected for drug formulation and further pre-clin. development.

L37 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of combretastatin A4 analogs as neoplasm inhibitors
AN 1993:101642 CAPLUS
DN 118:101642
TI Preparation of combretastatin A4 analogs as neoplasm inhibitors
IN Rathbone, Daniel Lee; Slack, John Alfred; Griffin, Roger John; Quarterman, Charmaine Paulina
PA Aston Molecules Ltd., UK
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9216486	A1	19921001	WO 1992-GB498	19920319
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
				GB 1991-6177	19910322
	AU 9213719	A1	19921021	AU 1992-13719	19920319
				GB 1991-6177	19910322
				WO 1992-GB498	19920319

OS MARPAT 118:101642
GI



I

II

AB Title compds. I [R1-R4 = alkoxy; Y = H, phosphate, phosphate derivative, amino acid carbamate, carbohydrate derivative, polyhydroxylated group] were prepared via Wittig olefination of benzaldehyde derivative II (X = protecting group) by a trialkoxybenzylphosphonium halide. I, e.g., water soluble combretastatin A4 analogs, are neoplasm inhibitors (no data). Thus, 3-hydroxy-4-methoxybenzaldehyde was protected by thexyldimethylsilyl chloride then olefinated by 3,4,5-trimethoxybenzylphosphonium bromide (preparation given). The product was deprotected by Bu4NF to give combretastatin A4. This was treated with di-tert-Bu N,N-diethylphosphoramidite and 1H-tetrazole in THF, cooled to -70°, then treated, with MCPBA to give combretastatin A4 phosphate bis(tert-butyl) ester in 77% yield.

=> phosphine
63579 PHOSPHINE

```
         14991 PHOSPHINES
L48      67690 PHOSPHINE
                (PHOSPHINE OR PHOSPHINES)

=> l37 and l48
L49          2 L37 AND L48

=> d l49 1-2 ti

L49  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation and formulation of combretastatin A4 prodrugs and their
     trans-isomers for use as antitumor agents

L49  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents. 389. New syntheses of the combretastatin A-4
     prodrug


=> d l49 1-2 ti fbib abs

L49  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation and formulation of combretastatin A4 prodrugs and their
     trans-isomers for use as antitumor agents
AN   1999:451301  CAPLUS
DN   131:73507
TI   Preparation and formulation of combretastatin A4 prodrugs and their
     trans-isomers for use as antitumor agents
IN   Pettit, George R.; Rhodes, Monte R.
PA   Arizona State University, USA
SO   PCT Int. Appl., 55 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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PI   WO 9935150            A1    19990715    WO 1999-US419            19990108
         W:  CA, JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
                                            US 1998-71070P      P    19980109
                                            US 1998-111531P     P    19981209
     CA 2314238             AA    19990715    CA 1999-2314238          19990108
                                            US 1998-71070P      P    19980109
                                            US 1998-111531P     P    19981209
                                            WO 1999-US419       W    19990108
     EP 1045853             A1    20001025    EP 1999-902121           19990108
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
                                            US 1998-71070P      P    19980109
                                            US 1998-111531P     P    19981209
                                            WO 1999-US419       W    19990108
     JP 2002500227          T2    20020108    JP 2000-527548           19990108
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                                            WO 1999-US419       W    19990108

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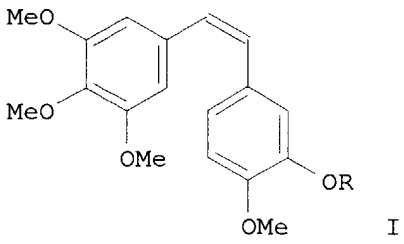
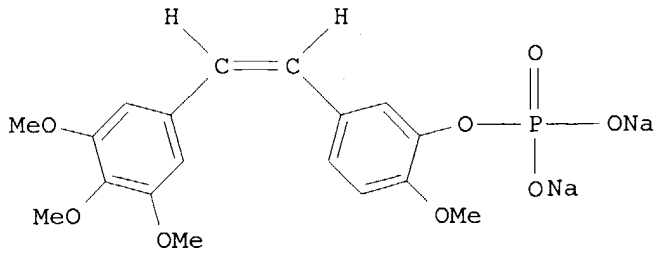


I

AB Combretastatin A4 I (R = H) and analogous phosphate prodrugs I [R = PO(OR1)OR2; R1, R2 = H, Na, Ca, Cs, Li, Mg, Mn, Zn, imidazole, morpholine, piperazine piperidine, pyrazole, pyridine, adenosine, cinchonine, glucosamine quinine, quinidine, tetracycline, verapamil; R1 = R2 = H, benzyl] and (E)-Combretastatin A4 phosphate analogs were prepared and formulated for use as water soluble antineoplastic agents. Thus, combretastatin A4 was reacted with dibenzyl phosphite to give dibenzyl ester I [R = P(O)(OCH2Ph)2] in 98% yield. Also, combretastatin A4 was converted to the sodium phosphate salt I [R = PO3HNa] via the formation of the silylethyl ester I [R = P(O)(OCH2CH2SiMe3)2]. The combretastatin A4 phosphate esters were tested for antitumor activity against a variety of cancer cell lines and were also tested for antimicrobial activity against bacterial and fungal strains.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents. 389. New syntheses of the combretastatin A-4 prodrug
AN 1998:301433 CAPLUS
DN 129:36213
TI Antineoplastic agents. 389. New syntheses of the combretastatin A-4 prodrug
AU Pettit, George R.; Rhodes, Monte R.
CS Cancer Research Institute and Department of Chemistry, Arizona State University, Tempe, AZ, 85287-2404, USA
SO Anti-Cancer Drug Design (1998), 13(3), 183-191
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal
LA English
GI



I

AB Combretastatin A-4 as the phosphate ester prodrug I is a potent antineoplastic and antiangiogenesis substance and is in advanced preclin. development. For the purpose of improving the phosphorylation synthetic sequence from combretastatin A-4, new routes were studied. The phosphorylation step is considerably improved using in situ-generated

dibenzyl chlorophosphite. Cleavage of the benzyl esters employing a trimethylchlorosilane/NaI procedure, followed by treatment with Na methoxide, led to the water-soluble prodrug I in high yield.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l37 1-9 ti

L37 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of resveratrol and sodium resverastatin phosphate derivatives for use in pharmaceutical compositions as antineoplastic and antimicrobial agents

L37 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of stilbenes as vascular targeting agents (VTAs) for treatment of solid tumors and retinal neovascularization.

L37 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis, in vitro, and in vivo evaluation of phosphate ester derivatives of combretastatin A-4

L37 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Combretastatin A-4 phosphate prodrug mono- and di-organic amine salts, mono- and di- amino acid salts, and mono- and di-amino acid ester salts

L37 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis of disodium combretastatin A-4 3'-O-phosphate

L37 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and use of cis-stilbene derivatives with vascular damaging activity

L37 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods of synthesizing prodrugs of combretastatin A-4

L37 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of combretastatin A4 prodrugs and their trans-isomers for use as antitumor agents

L37 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 393. Synthesis of the trans-isomer of combretastatin A-4 prodrug

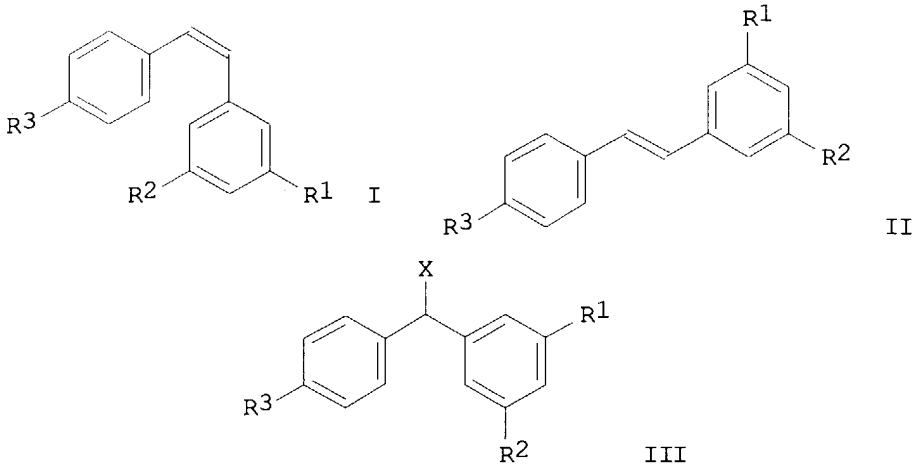
=> d l37 1 ti fbib abs

L37 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of resveratrol and sodium resverastatin phosphate derivatives for use in pharmaceutical compositions as antineoplastic and antimicrobial agents
AN 2003:836866 CAPLUS
DN 139:337828
TI Preparation of resveratrol and sodium resverastatin phosphate derivatives for use in pharmaceutical compositions as antineoplastic and antimicrobial agents
IN Pettit, George R.; Grealish, Matthew P.
PA Arizona Board of Regents, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086414	A1	20031023	WO 2003-US11008	20030410
	W: CA, JP, US				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
				US 2002-371782P	P 20020410

OS CASREACT 139:337828

GI



AB Combretastatin A-4, resveratrol, resverastatin, benzophenone and benzhydrol derivs. and analogs, such as I, II and III [R1, R2, R3 = OH, OMe; X = :O, OH], were prepared for therapeutic uses as antineoplastic and antimicrobial agents. Thus, (E)- and (Z)-3,5,4'-trimethoxystilbene were prepared in 91% overall yield via an olefination reaction of 4-methoxybenzyltriphenylphosphonium bromide and 3,5-dimethoxybenzaldehyde using BuLi in THF. The prepared compds. were assayed for inhibition of tubulin polymerization and colchicine binding and for activity against cancer cell lines, such as P388 leukemia and pancreas-a BXPC-3, and for activity against organisms, such as S. aureus, C. albicans and E. coli.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	55.27	403.12
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.60	-17.50

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 12:11:47 ON 27 SEP 2004

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Welcome to STN International!  Enter x:
LOGINID:SSSPTA1623PAZ

PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 12:41:52 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 12:41:52 ON 27 SEP 2004
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      55.27     403.12

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -5.60     -17.50

=> ?microb?
L50     419966 ?MICROB?

=> d his

     (FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

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               E COMBRETASTATIN A-4/CN
L1             1 E9
L2             1 E10

     FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004
L3            54 L1
L4            41 L2
L5            92 L3 OR L4
L6        410638 NUCLEOTIDE
L7             4 L5 AND L6
L8        281040 LITHIUM
L9             3 L5 AND L8
L10            8 L1/PREP

     FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
               DEL ALKYLATIN/L
               DEL ESTERODOR/L
               DEL GABACOMPDS/A
               DEL GORDSRCH/L
               DEL INDIUMCL3/A
               DEL LTWENTAUGFOR/A
               DEL NEOTAMECRYST/A
               DEL NVLARMFULGEN/A
               DEL POHBENZALDEH/A
               DEL PROSTACMPD15/A
               DEL STILLEAPP/L

     FILE 'REGISTRY' ENTERED AT 07:46:20 ON 27 SEP 2004
               E TETRABROMOMETHANE/CN
L11            1 E3
               E TETRACHLOROMOMETHANE/CN
               E TETRACHLOROMETHANE/CN
L12            1 E3
               E TETRAIODOMETHANE/CN
L13            1 E3

     FILE 'CAPLUS' ENTERED AT 07:48:31 ON 27 SEP 2004
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L14          2953 L11
L15         40657 L12
L16           325 L13
L17         42754 L14 OR L15 OR L16
L18         39583 ?PHOSPHITE
L19           207 L17 AND L18
L20           207 L17 AND L18
L21            52 L17(L)L18
L22             4 COMBRESTATIN
L23           437 COMBRETASTATIN
L24             0 L21 AND L23
L25            19 L23 AND L18
L26           207 L17 AND L19
L27            19 L18 AND L23

     FILE 'CAPLUS' ENTERED AT 08:14:50 ON 27 SEP 2004
L28            46 PHARMACEUTICAL S
L29         22284 TS
L30           157 PHARMACEUTICAL SALT
L31       1955208 REVIEW
L32             3 L30 AND L31

     FILE 'CAPLUS' ENTERED AT 09:25:19 ON 27 SEP 2004

     FILE 'REGISTRY' ENTERED AT 09:25:28 ON 27 SEP 2004
L33               STRUCTURE UPLOADED
L34             2 SEARCH L33 SSS SAM
L35            50 SEARCH L33 SSS FULL

     FILE 'CAPLUS' ENTERED AT 09:26:37 ON 27 SEP 2004
L36            98 L35
L37            15 L35/PREP
L38         39583 ?PHOSPHITE
L39             6 L37 AND L38
L40            27 NUCLOTIDE
L41        410638 NUCLEOTIDE
L42            29 L41 AND L23
L43             1 L41(L)L23

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L44             1 E3

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L45             3 L44 AND L17
L46           258 ATHERTON
L47             0 L23 AND L46
                 SAVE TEMP ALL COMBRETSRCH/L
L48         67690 PHOSPHINE
L49             2 L37 AND L48
L50        419966 ?MICROB?

=> l23(l)l50
L51            12 L23(L)L50

=> d l51 1-12 ti

L51  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of resveratrol and sodium resverastatin phosphate derivatives
     for use in pharmaceutical compositions as antineoplastic and antimicrobial
     agents
```

L51 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of **combretastatin** A-2 prodrugs as antitumor and **antimicrobial** agents

L51 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic Agents. 487. Synthesis and Biological Evaluation of the Antineoplastic Agent 3,4-Methylenedioxy-5,4'-dimethoxy-3'-amino-Z-stilbene and Derived Amino Acid Amides

L51 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms

L51 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 460. Synthesis of combretastatin A-2 prodrugs

L51 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic Agents. 465. Structural Modification of Resveratrol: Sodium Resverastatin Phosphate

L51 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antitubulin assembly and cell growth inhibitor denominated "dioxostatin"

L51 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis of hydroxyphenstatin and the prodrugs thereof as anticancer and antimicrobial agents

L51 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 463. Synthesis of combretastatin A-3 diphosphate prodrugs

L51 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic Agents 440. Asymmetric Synthesis and Evaluation of the Combretastatin A-1 SAR Probes (1S,2S)- and (1R,2R)-1,2-Dihydroxy-1-(2',3'-dihydroxy-4'-methoxyphenyl)-2-(3'',4'',5''-trimethoxyphenyl)-ethane

L51 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of combretastatin A4 prodrugs and their trans-isomers for use as antitumor agents

L51 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 393. Synthesis of the trans-isomer of combretastatin A-4 prodrug

=> d l51 12 ti fbib abs

L51 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 393. Synthesis of the trans-isomer of combretastatin A-4 prodrug
AN 1999:284035 CAPLUS
DN 131:82669
TI Antineoplastic agents 393. Synthesis of the trans-isomer of combretastatin A-4 prodrug
AU Pettit, George R.; Rhodes, Monte R.; Herald, Delbert L.; Chaplin, Dai J.; Stratford, Michael R. L.; Hamel, Ernest; Pettit, Robin K.; Chapuis, Jean-Charles; Oliva, Deanna
CS Cancer Research Institute and Department of Chemistry, Arizona State University, Tempe, AZ, 85287-2494, USA
SO Anti-Cancer Drug Design (1998), 13(8), 981-993
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press

DT Journal
LA English
AB The (E)-stilbene isomer (2a) of the (Z)-**combretastatin** A-4 prodrug (1b) was efficiently prepared from (E)-**combretastatin** A-4 by a reaction sequence employing phosphorylation (dibenzyl chlorophosphite), cleavage (trimethyliodosilane) of the benzyl ester and reaction of the resulting phosphoric acid with sodium methoxide. The sodium phosphate product (2c) was also found to be an important side-product, presumably from iodine-catalyzed isomerization, when the analogous synthetic route was used to obtain the **combretastatin** A-4 prodrug (1b). The phosphoric acid precursor of prodrug 1b derived from (Z)-**combretastatin** A-4 (1a) was converted into a series of metal cation and ammonium cation salts to evaluate effects on human cancer cell growth, **antimicrobial** activities and solubility behavior.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	66.00	413.85
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.30	-18.20

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 12:45:24 ON 27 SEP 2004

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LOGINID:SSSPTA1623PAZ

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 13:06:03 ON 27 SEP 2004
FILE 'CAPLUS' ENTERED AT 13:06:03 ON 27 SEP 2004
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	66.00	413.85
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.30	-18.20

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(FILE 'HOME' ENTERED AT 07:15:47 ON 27 SEP 2004)

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E COMBRETASTATIN A-4/CN
L1 1 E9
L2 1 E10

FILE 'CAPLUS' ENTERED AT 07:17:25 ON 27 SEP 2004

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L3            54 L1
L4            41 L2
L5            92 L3 OR L4
L6        410638 NUCLEOTIDE
L7             4 L5 AND L6
L8        281040 LITHIUM
L9             3 L5 AND L8
L10            8 L1/PREP

      FILE 'STNGUIDE' ENTERED AT 07:44:04 ON 27 SEP 2004
                  DEL ALKYLATIN/L
                  DEL ESTERODOR/L
                  DEL GABACOMPDS/A
                  DEL GORDSRCH/L
                  DEL INDIUMCL3/A
                  DEL LTWENTAUGFOR/A
                  DEL NEOTAMECRYST/A
                  DEL NVLARMFULGEN/A
                  DEL POHBENZALDEH/A
                  DEL PROSTACMPD15/A
                  DEL STILLEAPP/L

      FILE 'REGISTRY' ENTERED AT 07:46:20 ON 27 SEP 2004
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L11             1 E3
                  E TETRACHLOROMOMETHANE/CN
                  E TETRACHLOROMETHANE/CN
L12             1 E3
                  E TETRAIODOMETHANE/CN
L13             1 E3

      FILE 'CAPLUS' ENTERED AT 07:48:31 ON 27 SEP 2004
L14          2953 L11
L15         40657 L12
L16           325 L13
L17         42754 L14 OR L15 OR L16
L18         39583 ?PHOSPHITE
L19           207 L17 AND L18
L20           207 L17 AND L18
L21            52 L17(L)L18
L22             4 COMBRESTATIN
L23           437 COMBRETASTATIN
L24             0 L21 AND L23
L25            19 L23 AND L18
L26           207 L17 AND L19
L27            19 L18 AND L23

      FILE 'CAPLUS' ENTERED AT 08:14:50 ON 27 SEP 2004
L28            46 PHARMACEUTICAL S
L29         22284 TS
L30           157 PHARMACEUTICAL SALT
L31       1955208 REVIEW
L32             3 L30 AND L31

      FILE 'CAPLUS' ENTERED AT 09:25:19 ON 27 SEP 2004

      FILE 'REGISTRY' ENTERED AT 09:25:28 ON 27 SEP 2004
L33               STRUCTURE UPLOADED
L34             2 SEARCH L33 SSS SAM
L35            50 SEARCH L33 SSS FULL

      FILE 'CAPLUS' ENTERED AT 09:26:37 ON 27 SEP 2004
L36            98 L35
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L37          15 L35/PREP
L38       39583 ?PHOSPHITE
L39           6 L37 AND L38
L40          27 NUCLOTIDE
L41      410638 NUCLEOTIDE
L42          29 L41 AND L23
L43           1 L41(L)L23

     FILE 'REGISTRY' ENTERED AT 10:17:01 ON 27 SEP 2004
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               E DIBENZYL PHOSPHITE/CN
L44           1 E3

     FILE 'CAPLUS' ENTERED AT 10:17:51 ON 27 SEP 2004
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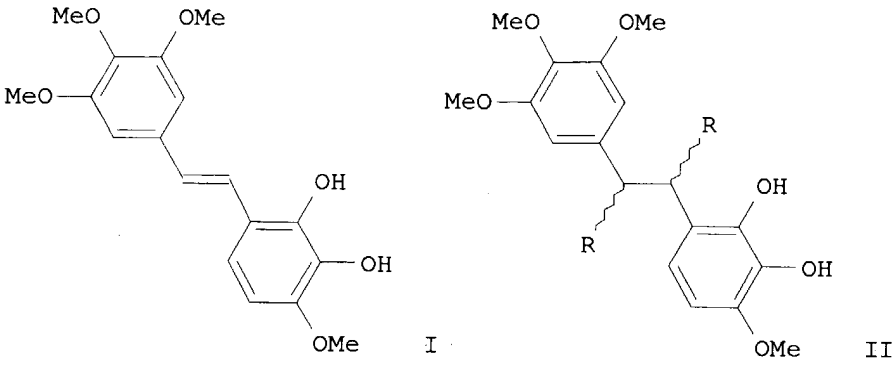
L46         258 ATHERTON
L47           0 L23 AND L46
               SAVE TEMP ALL COMBRETSRCH/L
L48       67690 PHOSPHINE
L49           2 L37 AND L48
L50      419966 ?MICROB?
L51          12 L23(L)L50

=> d l51 9-12 ti fbib abs

L51  ANSWER 9 OF 12  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic agents 463. Synthesis of combretastatin A-3 diphosphate
     prodrugs
AN   2001:612313  CAPLUS
DN   136:31380
TI   Antineoplastic agents 463. Synthesis of combretastatin A-3 diphosphate
     prodrugs
AU   Pettit, George R.; Minardi, Mathew D.; Boyd, Michael R.; Pettit, Robin K.
CS   Cancer Research Institute and Department of Chemistry and Biochemistry,
     Arizona State University, Tempe, AZ, 85287-2404, USA
SO   Anti-Cancer Drug Design (2001), Volume Date 2000, 15(6), 397-403
     CODEN: ACDDEA; ISSN: 0266-9536
PB   Oxford University Press
DT   Journal
LA   English
AB   A new and more efficient synthesis of combretastatin A-3 was
     completed (8.4% overall yield) starting from Me gallate and isovanillin
     with aldehyde and phosphonium salt as key intermediates. Conversion of
     combretastatin A-3 to a series of diphosphate prodrugs was readily
     achieved. Both the diphosphate sodium and potassium salts displayed aqueous
     solubility in excess of 220 mg/mL at room temperature and good cancer cell line
     inhibitory activity. The combretastatins were shown to be
     moderately antimicrobial against bacteria and fungi.
RE.CNT  33    THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51  ANSWER 10 OF 12  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Antineoplastic Agents 440. Asymmetric Synthesis and Evaluation of the
     Combretastatin A-1 SAR Probes (1S,2S)- and (1R,2R)-1,2-Dihydroxy-
     1-(2',3'-dihydroxy-4'-methoxyphenyl)-2-(3'',4'',5''-trimethoxyphenyl)-
     ethane
AN   2000:443011  CAPLUS
DN   133:207722
TI   Antineoplastic Agents 440. Asymmetric Synthesis and Evaluation of the
     Combretastatin A-1 SAR Probes (1S,2S)- and (1R,2R)-1,2-Dihydroxy-
     1-(2',3'-dihydroxy-4'-methoxyphenyl)-2-(3'',4'',5''-trimethoxyphenyl)-
     ethane
AU   Pettit, George R.; Lippert, John W., III; Herald, Delbert L.; Hamel,
```

Ernest; Pettit, Robin K.
CS Cancer Research Institute and Department of Chemistry, Arizona State University, Tempe, AZ, 85287-2404, USA
SO Journal of Natural Products (2000), 63(7), 969-974
CODEN: JNPRDF; ISSN: 0163-3864
PB American Chemical Society
DT Journal
LA English
GI



AB The synthetic (E)-isomer (I) of natural combretastatin A-1 isolated from the African bushwillow Combretum caffrum was the focus of chiral hydroxylation (Sharpless) reactions as part of a structure-activity relationship study. The resulting (R,R)- (II; R = α-OH) (III) and (S,S,)-diols II (R = β-OH) (IV) and synthetic intermediates were evaluated against a series of cancer cell lines, microorganisms, and tubulin. Chiral diols III and IV showed increased activity against the P-388 murine lymphocytic leukemia cell line with ED50 values of 3.9 and 2.9 μg/mL, resp., when compared to the precursor (E)-stilbene I. In contrast, I exhibited more potent antibiotic activity than the chiral diols, III and IV. Both diols, III and IV, displayed less cancer cell growth inhibition and less antibiotic activity than did natural combretastatin A-1 (P-388 ED50 0.25 μg/mL).
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and formulation of combretastatin A4 prodrugs and their trans-isomers for use as antitumor agents
AN 1999:451301 CAPLUS
DN 131:73507
TI Preparation and formulation of combretastatin A4 prodrugs and their trans-isomers for use as antitumor agents
IN Pettit, George R.; Rhodes, Monte R.
PA Arizona State University, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9935150	A1	19990715	WO 1999-US419	19990108

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

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			US 1998-111531P	P	19981209
CA 2314238	AA	19990715	CA 1999-2314238		19990108
			US 1998-71070P	P	19980109
			US 1998-111531P	P	19981209
			WO 1999-US419	W	19990108
EP 1045853	A1	20001025	EP 1999-902121		19990108
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			US 1998-71070P	P	19980109
			US 1998-111531P	P	19981209
			WO 1999-US419	W	19990108
JP 2002500227	T2	20020108	JP 2000-527548		19990108
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			US 1998-111531P	P	19981209
			WO 1999-US419	W	19990108

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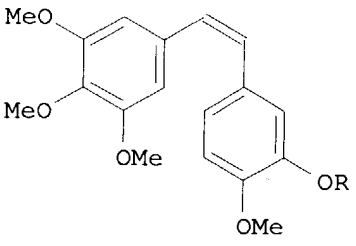

I

AB **Combretastatin** A4 I (R = H) and analogous phosphate prodrugs I [R = PO(OR1)OR2; R1, R2 = H, Na, Ca, Cs, Li, Mg, Mn, Zn, imidazole, morpholine, piperazine piperidine, pyrazole, pyridine, adenosine, cinchonine, glucosamine quinine, quinidine, tetracycline, verapamil; R1 = R2 = H, benzyl] and (E)-**Combretastatin** A4 phosphate analogs were prepared and formulated for use as water soluble antineoplastic agents. Thus, **combretastatin** A4 was reacted with dibenzyl phosphite to give dibenzyl ester I [R = P(O)(OCH2Ph)2] in 98% yield. Also, **combretastatin** A4 was converted to the sodium phosphate salt I [R = PO3HNa] via the formation of the silylethyl ester I [R = P(O)(OCH2CH2SiMe3)2]. The **combretastatin** A4 phosphate esters were tested for antitumor activity against a variety of cancer cell lines and were also tested for **antimicrobial** activity against bacterial and fungal strains.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antineoplastic agents 393. Synthesis of the trans-isomer of combretastatin A-4 prodrug
AN 1999:284035 CAPLUS
DN 131:82669
TI Antineoplastic agents 393. Synthesis of the trans-isomer of combretastatin A-4 prodrug
AU Pettit, George R.; Rhodes, Monte R.; Herald, Delbert L.; Chaplin, Dai J.; Stratford, Michael R. L.; Hamel, Ernest; Pettit, Robin K.; Chapuis, Jean-Charles; Oliva, Deanna
CS Cancer Research Institute and Department of Chemistry, Arizona State University, Tempe, AZ, 85287-2494, USA
SO Anti-Cancer Drug Design (1998), 13(8), 981-993
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal

LA English
AB The (E)-stilbene isomer (2a) of the (Z)-**combretastatin** A-4 prodrug (1b) was efficiently prepared from (E)-**combretastatin** A-4 by a reaction sequence employing phosphorylation (dibenzyl chlorophosphite), cleavage (trimethyliodosilane) of the benzyl ester and reaction of the resulting phosphoric acid with sodium methoxide. The sodium phosphate product (2c) was also found to be an important side-product, presumably from iodine-catalyzed isomerization, when the analogous synthetic route was used to obtain the **combretastatin** A-4 prodrug (1b). The phosphoric acid precursor of prodrug 1b derived from (Z)-**combretastatin** A-4 (1a) was converted into a series of metal cation and ammonium cation salts to evaluate effects on human cancer cell growth, **antimicrobial** activities and solubility behavior.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	81.04	428.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.10	-21.00

FILE 'STNGUIDE' ENTERED AT 13:12:31 ON 27 SEP 2004
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 24, 2004 (20040924/UP).

=> DIS SAVED

NAME	CREATED	NOTES/TITLE
COMBRETSRCH/L	TEMP	47 L-NUMBERS
TWOAMINOPOLY/Q	16 APR 2001	UPLOADED STRUCTURE

=> DIS SAVED/S
NO SAVED SDI REQUESTS

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'COMBRETSRCH/L' IN USE
A single name cannot be used for two saved items at the same time. Enter "Y" if you wish to replace the current saved name with a new definition. Enter "N" if the current saved definition must be preserved. You may then reenter the SAVE command with a different saved name. Enter "DISPLAY SAVED" at an arrow prompt (=>) to see a list of your currently defined saved names.
REPLACE OLD DEFINITION? Y/(N):y
L# LIST L1-L51 HAS BEEN SAVED AS 'COMBRETSRCH/L'

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.18	429.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE 0.00 -21.00

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:14:21 ON 27 SEP 2004